

10/513699

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEAL1624

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 11:28:57 ON 01 FEB 2008
FILE 'CAPLUS' ENTERED AT 11:28:57 ON 01 FEB 2008
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COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	103.89	282.46

	SINCE FILE	TOTAL
	ENTRY	SESSION
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		
CA SUBSCRIBER PRICE	-13.60	-13.60

=> file casreact
COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	104.85	283.42

	SINCE FILE	TOTAL
	ENTRY	SESSION
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		
CA SUBSCRIBER PRICE	-13.60	-13.60

FILE 'CASREACT' ENTERED AT 11:30:01 ON 01 FEB 2008
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FILE CONTENT:1840 - 26 Jan 2008 VOL 148 ISS 5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

* CASREACT now has more than 13.8 million reactions *
* *

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

<12/04/2007>

Erich Leese

10/513699

=>

Uploading C:\Program Files\Stnexp\Queries\10524517last.str



chain nodes :
7 8 9 11 12 14 15 18 19 20 21
ring nodes :
1 2 3 4 5 6
ring/chain nodes :
16 22
chain bonds :
1-7 2-15 3-14 5-11 6-12 7-8 7-9 9-16 18-19 18-22 19-20 19-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 1-7 2-3 2-15 3-4 3-14 4-5 5-6 5-11 6-12 7-8 7-9 9-16 18-19
18-22 19-21
exact bonds :
19-20
isolated ring systems :
containing 1 :

G1:C,H,O,X

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 11:CLASS
12:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 18

L5 STRUCTURE UPLOADED

<12/04/2007>

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=> s 15

SAMPLE SEARCH INITIATED 11:30:31 FILE 'CASREACT'
SCREENING COMPLETE - 502 REACTIONS TO VERIFY FROM 24 DOCUMENTS

100.0% DONE 502 VERIFIED 101 HIT RXNS 10 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 8697 TO 11383
PROJECTED ANSWERS: 11 TO 389

L6 10 SEA SSS SAM L5 (101 REACTIONS)

=> s 15 full

FULL SEARCH INITIATED 11:30:50 FILE 'CASREACT'
SCREENING COMPLETE - 8697 REACTIONS TO VERIFY FROM 561 DOCUMENTS

100.0% DONE 8697 VERIFIED 1974 HIT RXNS 197 DOCS
SEARCH TIME: 00.00.02

L7 197 SEA SSS FUL L5 (1974 REACTIONS)

=> s 17 and py<2003

486994 PY<2003

L8 93 L7 AND PY<2003

=> s 18 and organic solvent

12293 ORGANIC
21 ORGANICS
12313 ORGANIC
(ORGANIC OR ORGANICS)
62178 SOLVENT
18894 SOLVENTS
71620 SOLVENT
(SOLVENT OR SOLVENTS)
743 ORGANIC SOLVENT
(ORGANIC(W) SOLVENT)

L9 0 L8 AND ORGANIC SOLVENT

=> s 18 and solvent

62178 SOLVENT
18894 SOLVENTS
71620 SOLVENT
(SOLVENT OR SOLVENTS)

L10 1 L8 AND SOLVENT

=> d ibib abs hit

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L10 ANSWER 1 OF 1 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 138:55769 CASREACT

TITLE: Synthesis of potent and highly selective inhibitors of human tryptase

AUTHOR(S): Slusarchyk, William A.; Bolton, Scott A.; Hartl, Karen S.; Huang, Ming-Hsing; Jacobs, Glenn; Meng, Wei; Ogletree, Martin L.; Pi, Zulan; Schumacher, William A.; Seiler, Steven M.; Sutton, James C.; Treuner, Uwe; Zahler, Robert; Zhao, Guohua; Bisacchi, Gregory S.

CORPORATE SOURCE: The Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3235-3238

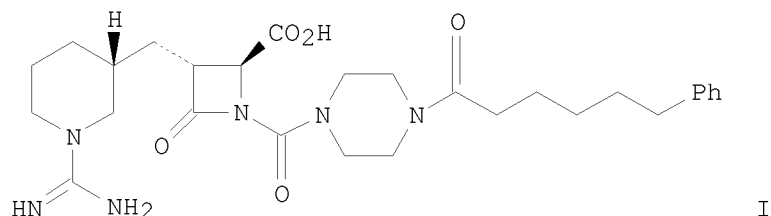
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

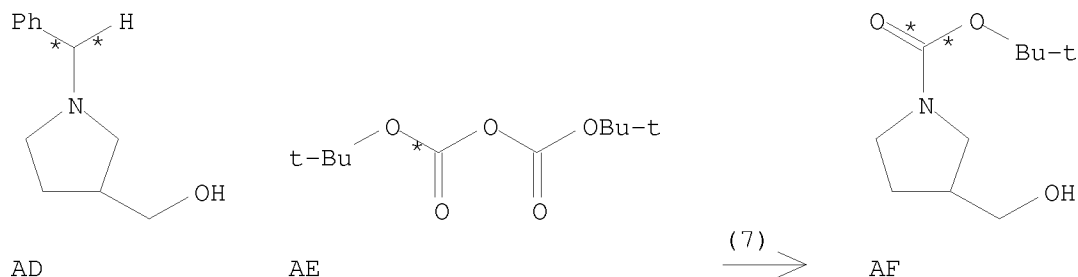
GI



AB The serine protease tryptase is implicated in allergic and inflammatory diseases and associated with asthma. The synthesis and SAR of a series of N1-activated-4-carboxy azetidinones are described, resulting in identification of BMS-363131 (I) as a potent inhibitor of human tryptase (IC₅₀<1.7 nM) with high selectivity (>3000-fold) for tryptase vs. related serine proteases including trypsin.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(7) OF 275 AD + AE ==> AF...



RX(7) RCT AD 5731-17-9

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STAGE(1)

RGT S 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

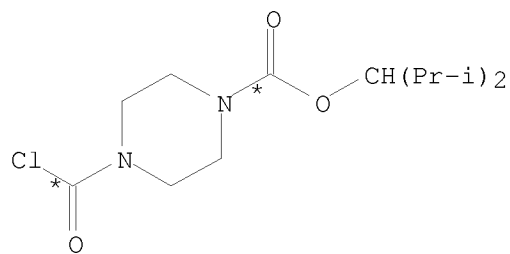
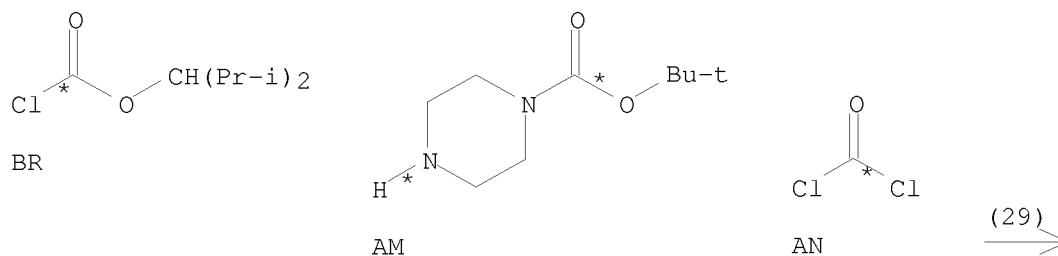
STAGE(2)

RCT AE 24424-99-5
SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(29) OF 275 BR + AM + AN ==> P...



P

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N

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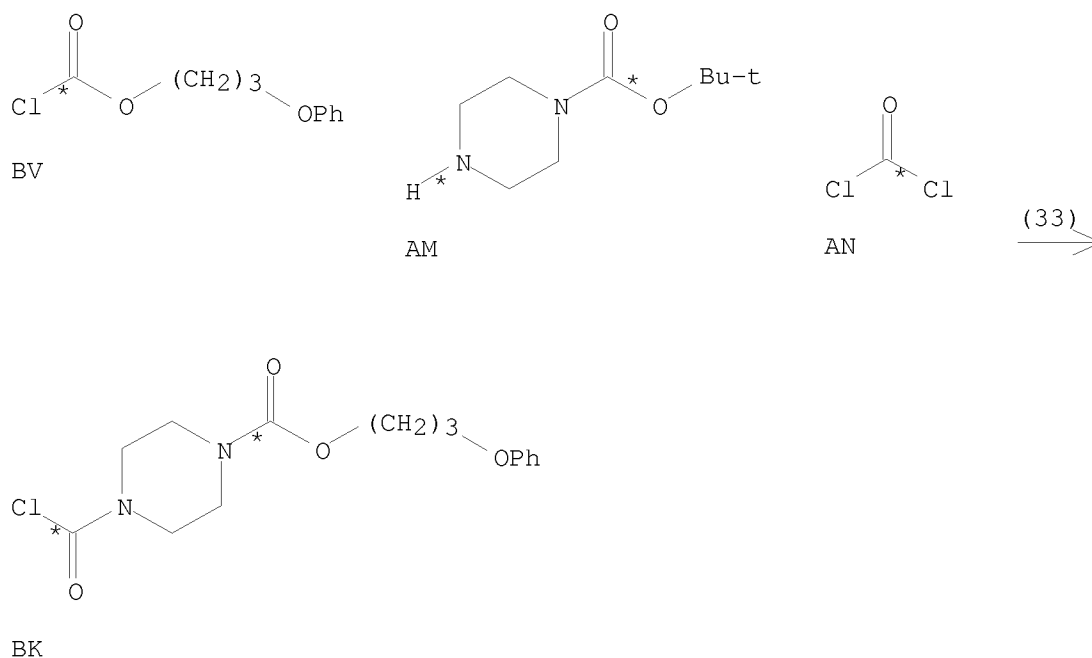
10/513699

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(33) OF 275 BV + AM + AN ==> BK...



RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

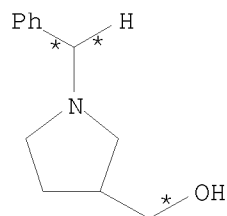
RX(50) OF 275 COMPOSED OF RX(7), RX(8)

RX(50) AD + AE ==> AH

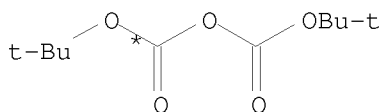
<12/04/2007>

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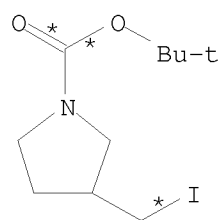


AD



AE

2
STEPS
→



AH

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2

CAT 7440-05-3 Pd

SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5

SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6

RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole

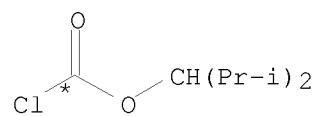
PRO AH 479622-36-1

SOL 75-09-2 CH₂Cl₂

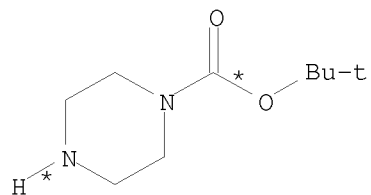
RX(75) OF 275 COMPOSED OF RX(29), RX(4)

RX(75) BR + AM + AN + L ==> Q

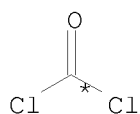
10/513699



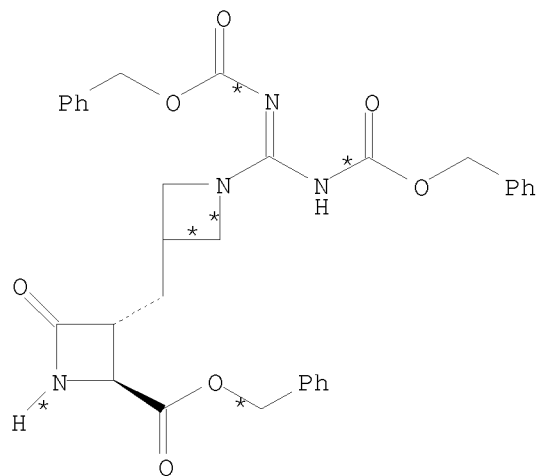
BR



AM



AN



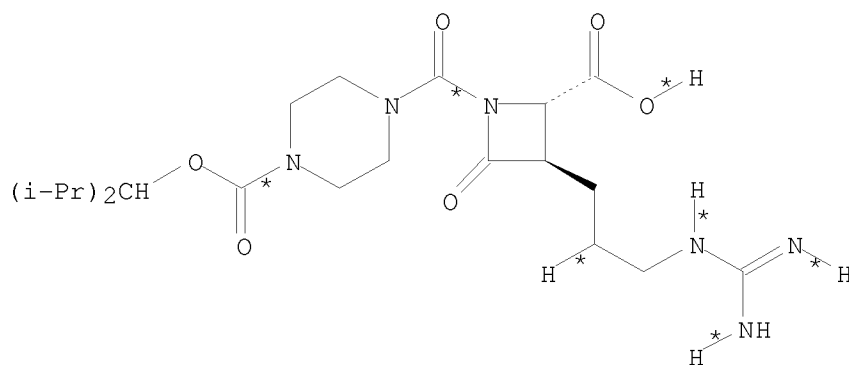
L

2
STEPS
→

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Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Q 253173-70-5

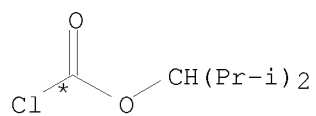
RX(76) OF 275 COMPOSED OF RX(29), RX(5)

RX(76) BR + AM + AN + X ==> Y

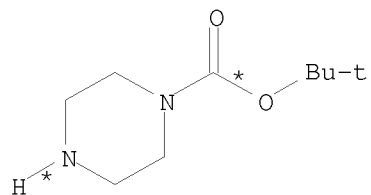
<12/04/2007>

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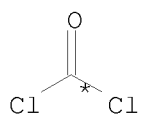
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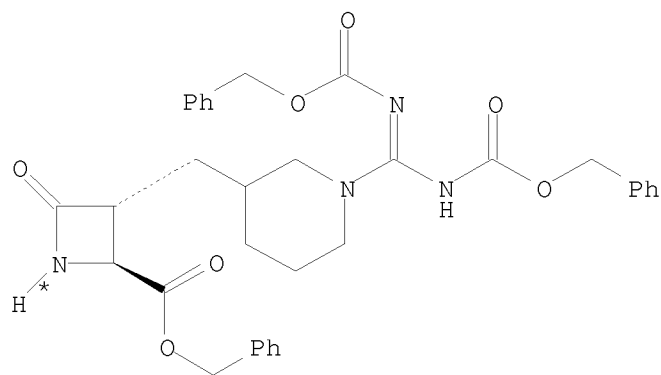
BR



AM



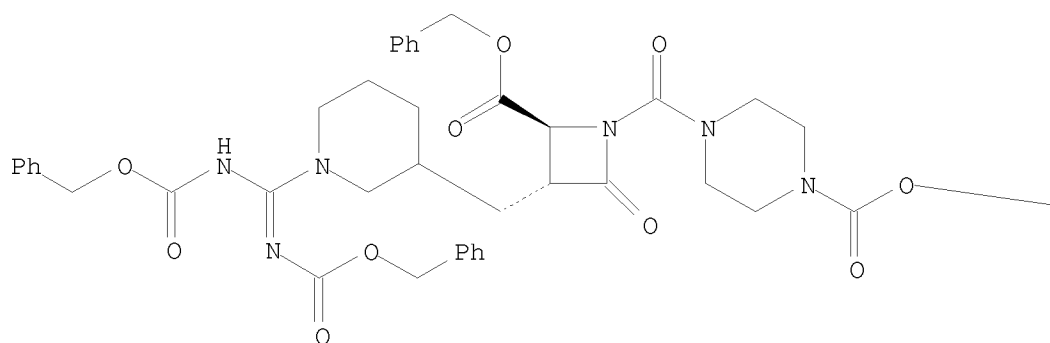
AN



X

2
STEPS
→

PAGE 1-A



<12/04/2007>

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—CH(Pr-i)₂

Y
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

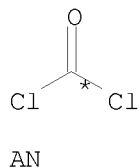
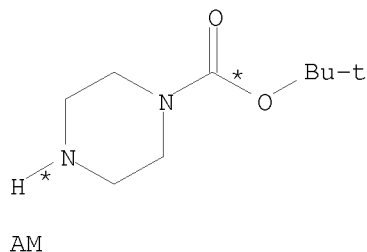
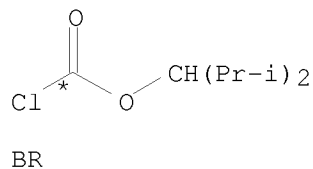
PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

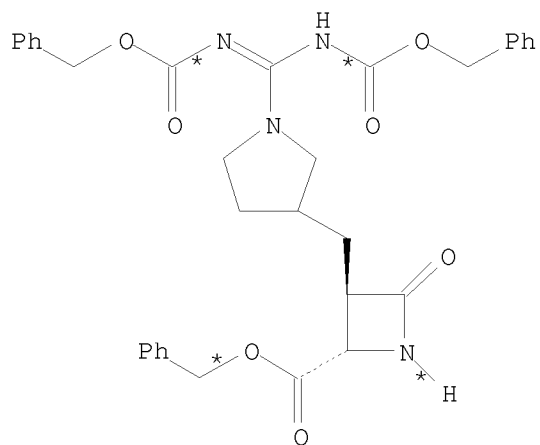
RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et₃N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(77) OF 275 COMPOSED OF RX(29), RX(20)

RX(77) BR + AM + AN + BA ==> BB

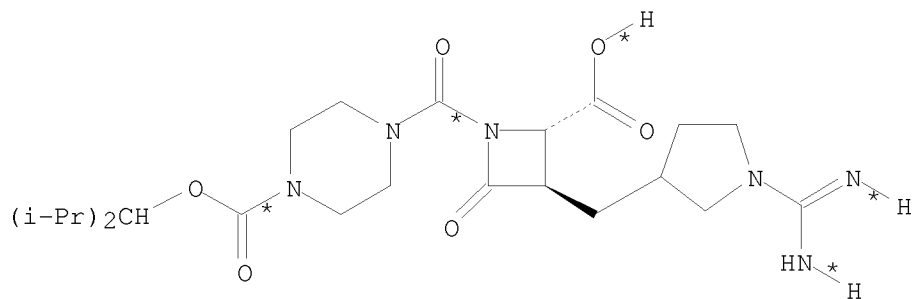


10/513699



BA

2
STEPS
→



BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

<12/04/2007>

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NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

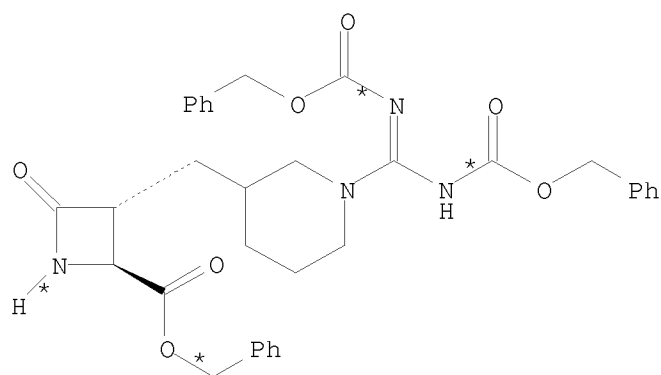
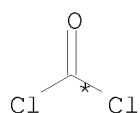
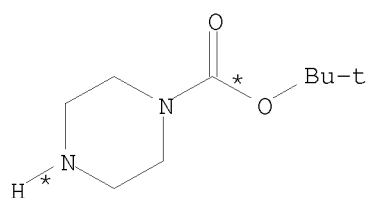
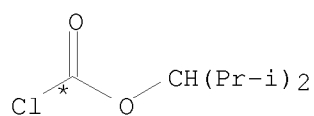
STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

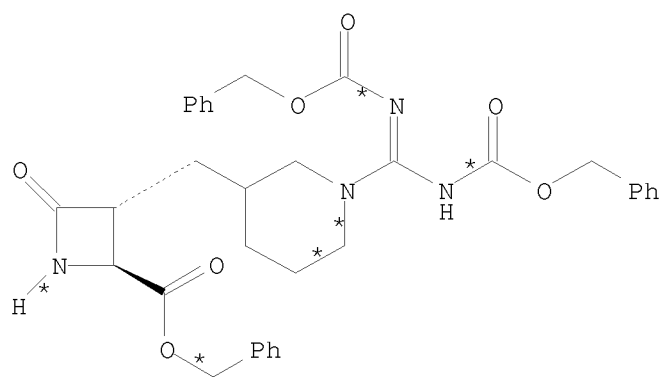
PRO BB 479622-24-7

RX(78) OF 275 COMPOSED OF RX(29), RX(21)

RX(78) 4 BR + 4 AM + 4 AN + 4 X ==> BB + BC
+ BD + BE

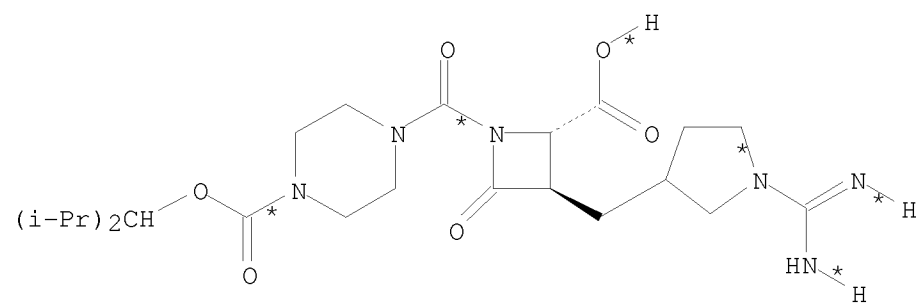


10/513699

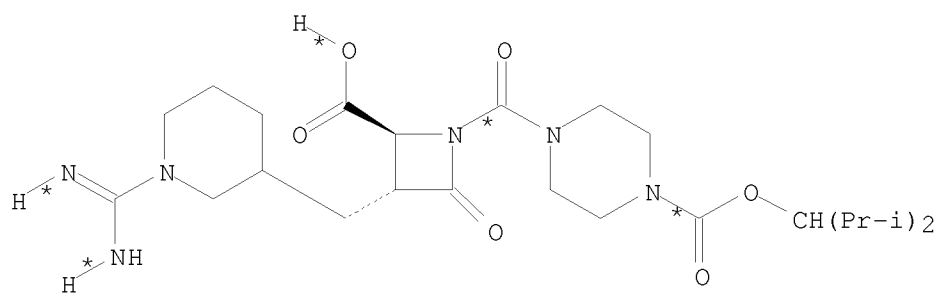


X

2
STEPS
→



BB

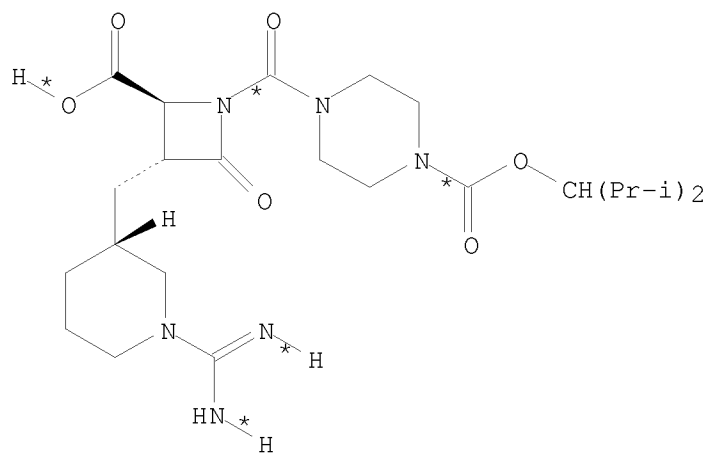


BC

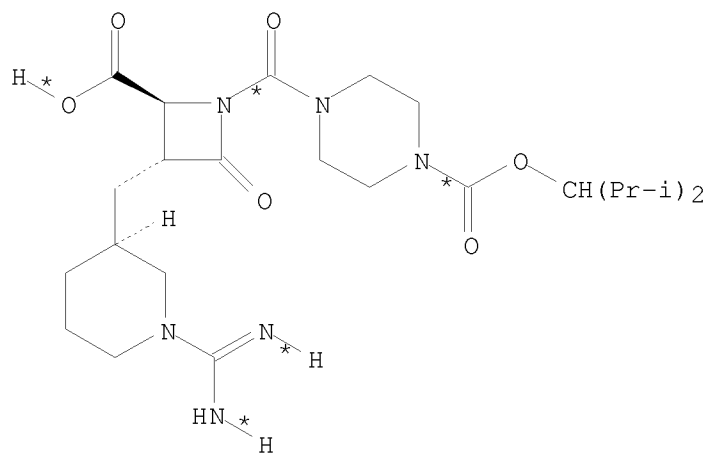
<12/04/2007>

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10/513699



BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N

<12/04/2007>

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10/513699

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

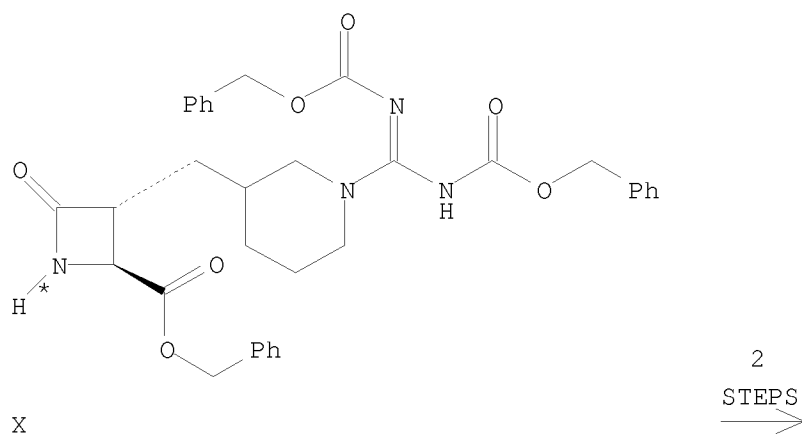
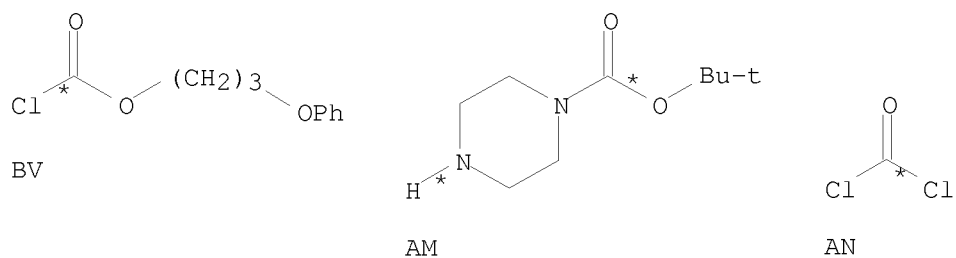
CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE
479622-26-9

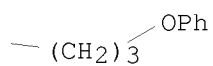
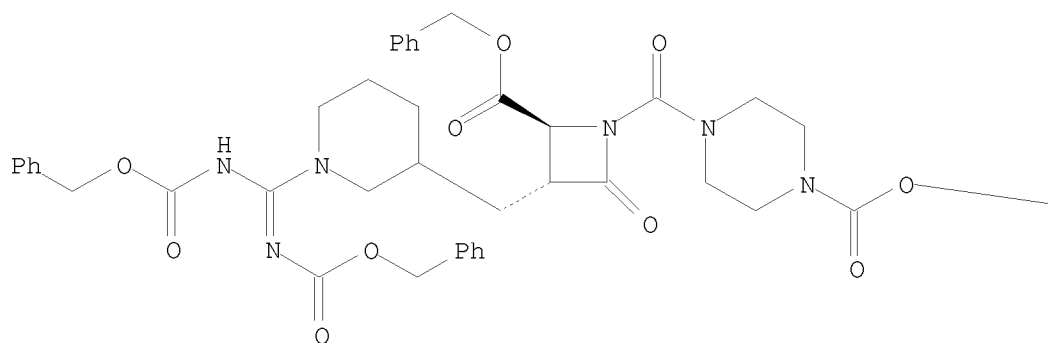
RX(84) OF 275 COMPOSED OF RX(33), RX(25)

RX(84) BV + AM + AN + X ==> BL



<12/04/2007>

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BL
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N

PRO BL 384830-26-6

CAT 1122-58-3 4-DMAP

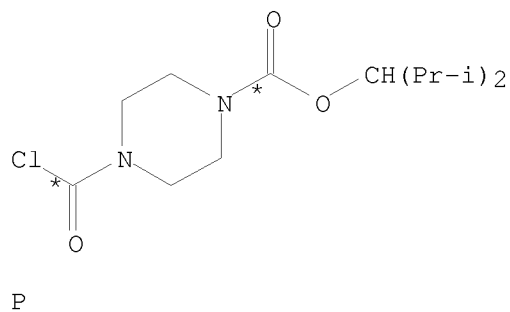
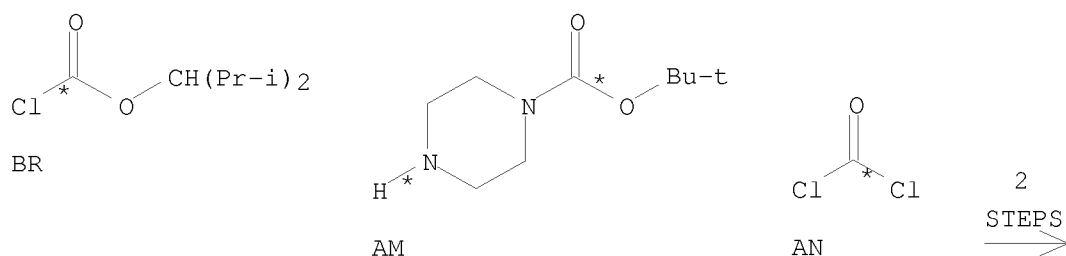
SOL 68-12-2 DMF

10/513699

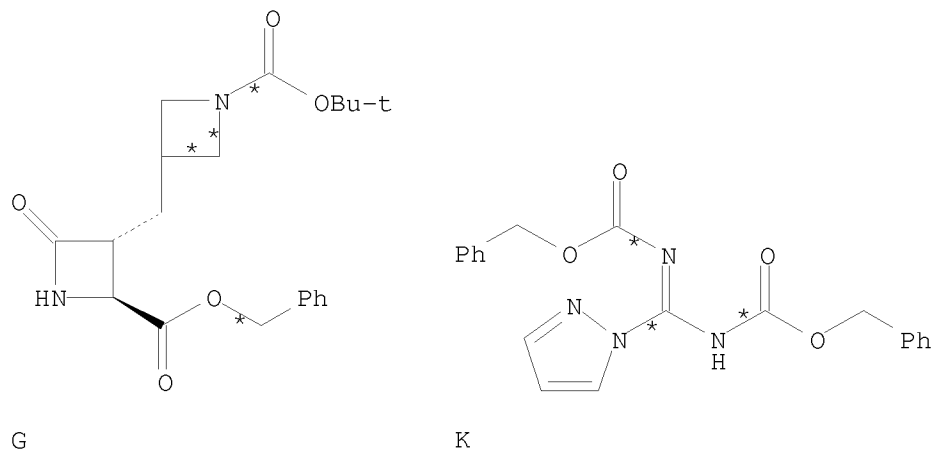
RX(93) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)
AND REACTION SEQUENCE RX(3), RX(4)

... BR + AM + AN ==> P...

...G + K + P ==> Q



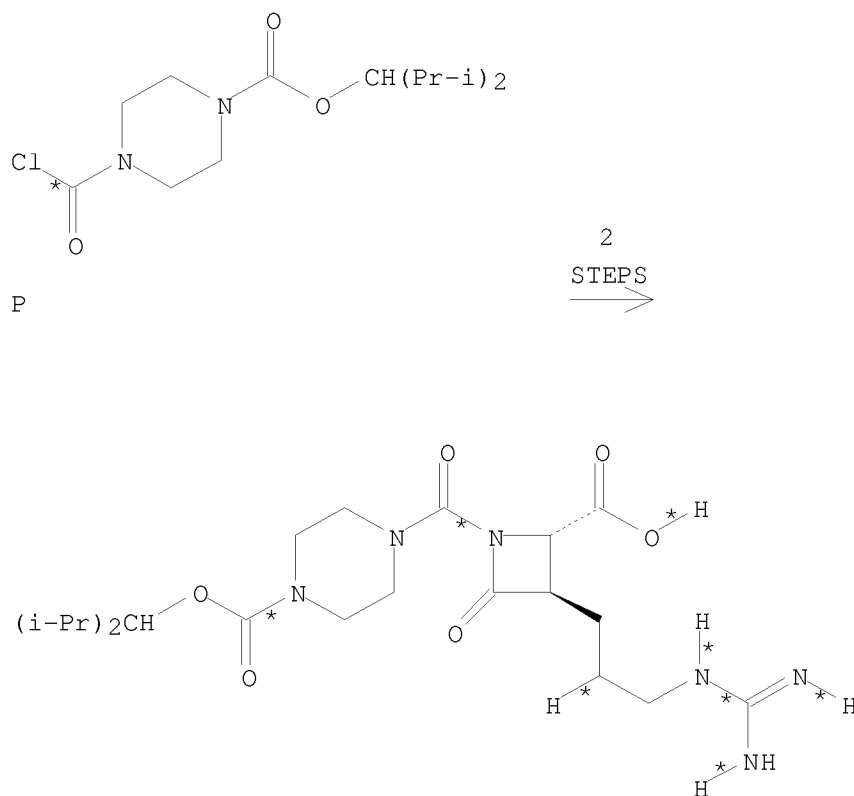
START NEXT REACTION SEQUENCE



<12/04/2007>

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10/513699



Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(3) RCT G 253176-97-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

<12/04/2007>

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10/513699

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO L 253177-00-3

NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

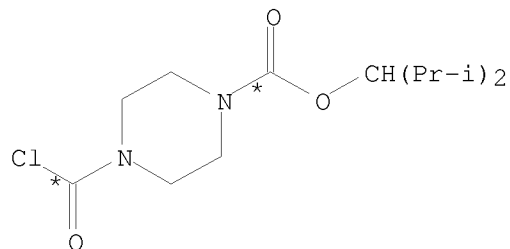
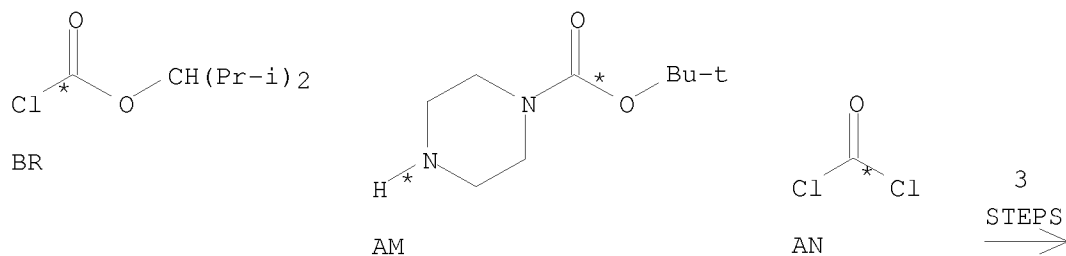
PRO Q 253173-70-5

RX(94) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)

AND REACTION SEQUENCE RX(2), RX(3), RX(4)

... BR + AM + AN ==> P...

...C + F + K + P ==> Q



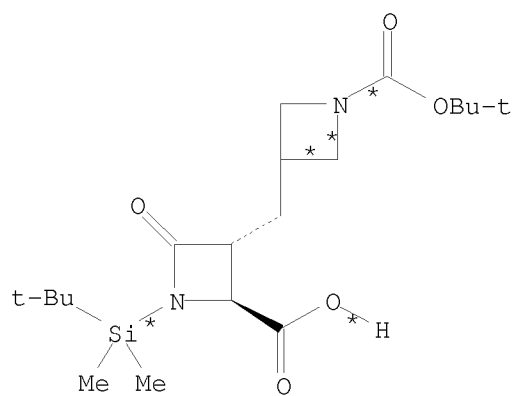
P

START NEXT REACTION SEQUENCE

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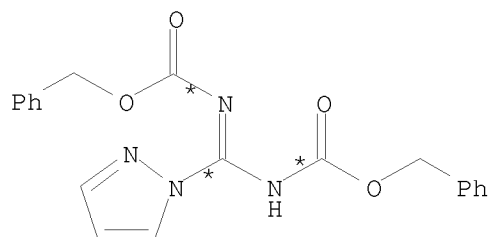
10/513699



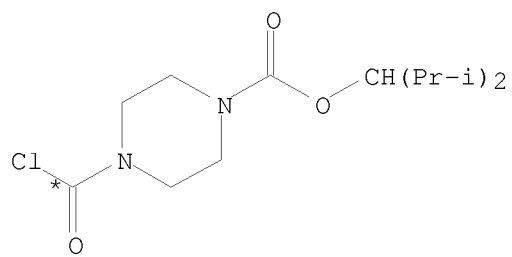
C



F



K



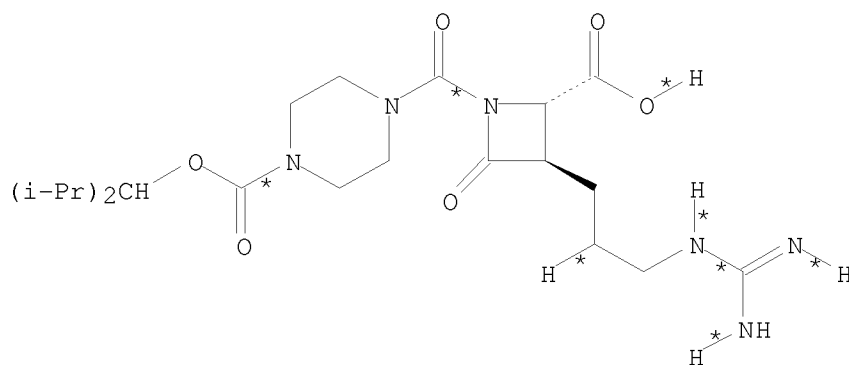
P

3
STEPS
→

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Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(2) RCT C 253176-95-3

STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

SOL 68-12-2 DMF

PRO G 253176-97-5

RX(3) RCT G 253176-97-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

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STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO L 253177-00-3
NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

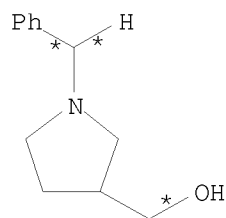
STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

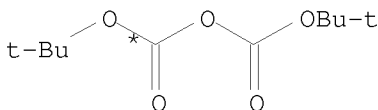
PRO Q 253173-70-5

RX(96) OF 275 COMPOSED OF RX(7), RX(8), RX(43)

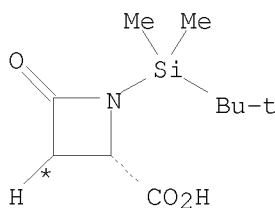
RX(96) AD + AE + B ==> AX



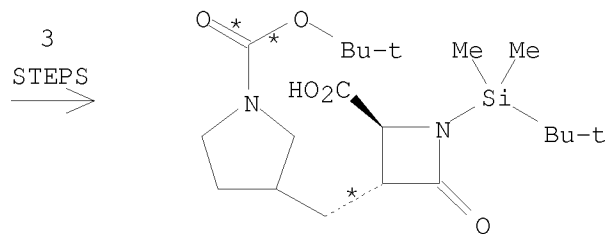
AD



AE



B



AX

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2
CAT 7440-05-3 Pd

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SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5

SOL 109-99-9 THF

PRO AF 114214-69-6

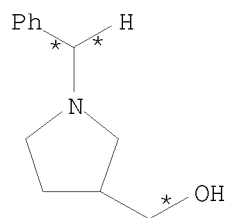
NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AH 479622-36-1
SOL 75-09-2 CH2Cl2

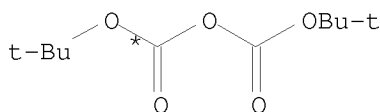
RX(43) RCT AH 479622-36-1, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AX 479622-21-4
SOL 109-99-9 THF
NTE stereoselective

RX(98) OF 275 COMPOSED OF RX(7), RX(8), RX(43), RX(16)

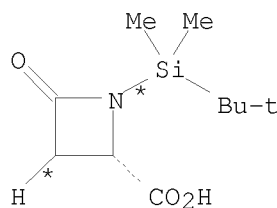
RX(98) AD + AE + B + F ==> AY



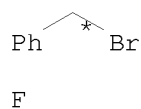
AD



AE

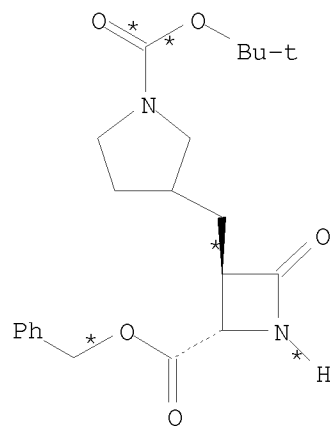


B



F

4
STEPS
=>



AY

10/513699

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2

CAT 7440-05-3 Pd

SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5

SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6

RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole

PRO AH 479622-36-1

SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

PRO AX 479622-21-4

SOL 109-99-9 THF

NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

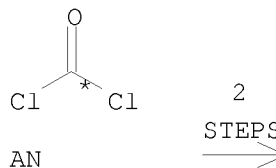
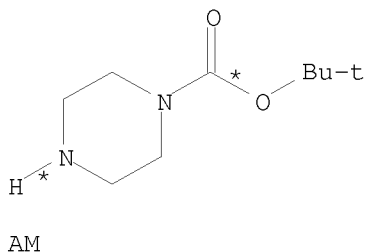
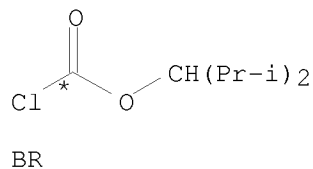
SOL 68-12-2 DMF

PRO AY 479622-22-5

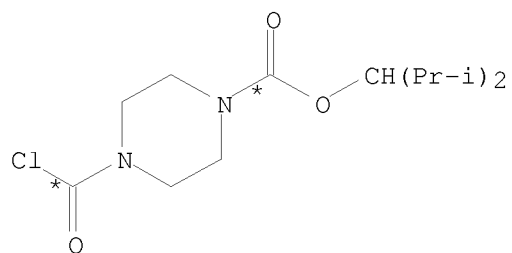
RX(124) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)
AND REACTION SEQUENCE RX(18), RX(20)

... BR + AM + AN ==> P...

...AY + K + P ==> BB

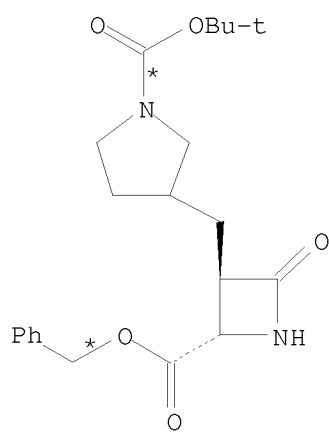


10/513699

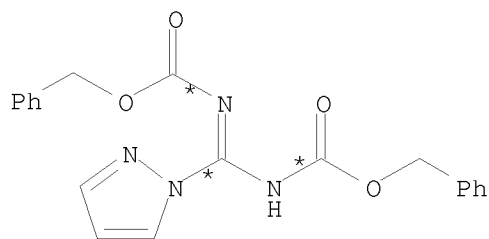


P

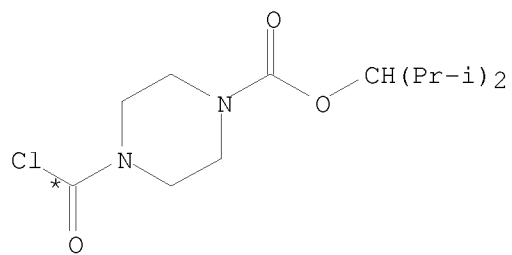
START NEXT REACTION SEQUENCE



AY



K



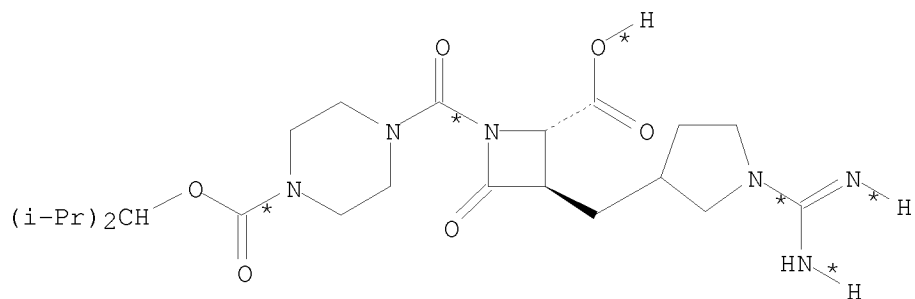
P

2
STEPS
→

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BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(18) RCT AY 479622-22-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO BA 479622-23-6

NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

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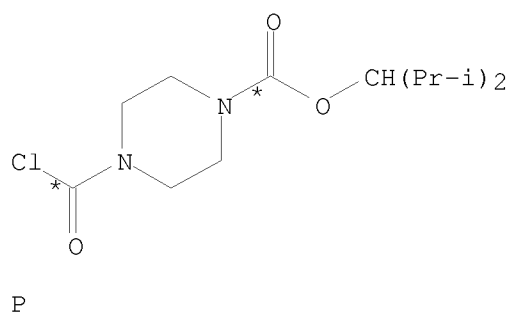
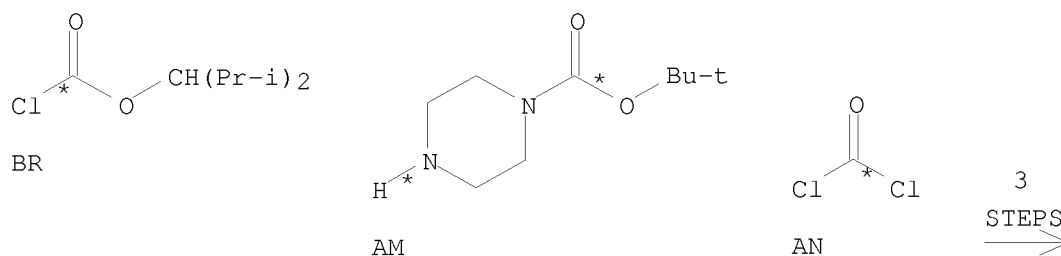
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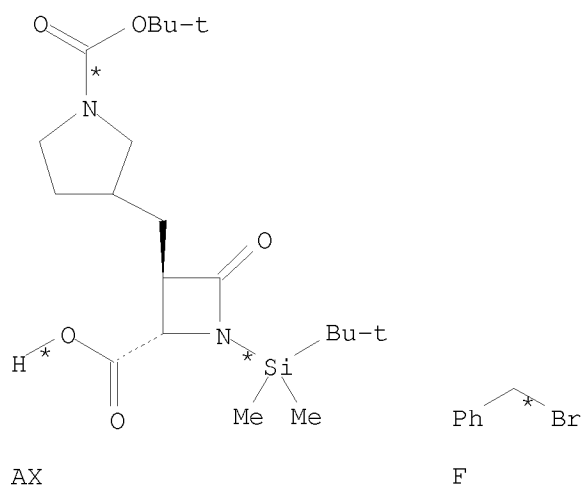
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

RX(125) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)
AND REACTION SEQUENCE RX(16), RX(18), RX(20)
... BR + AM + AN ==> P...
...AX + F + K + P ==> BB



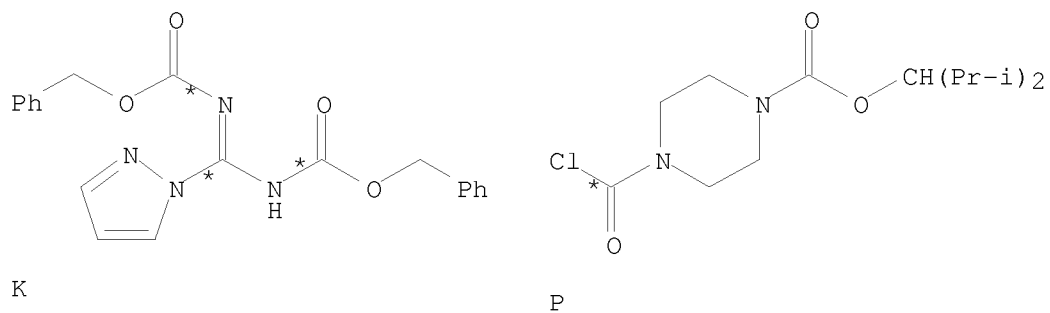
START NEXT REACTION SEQUENCE



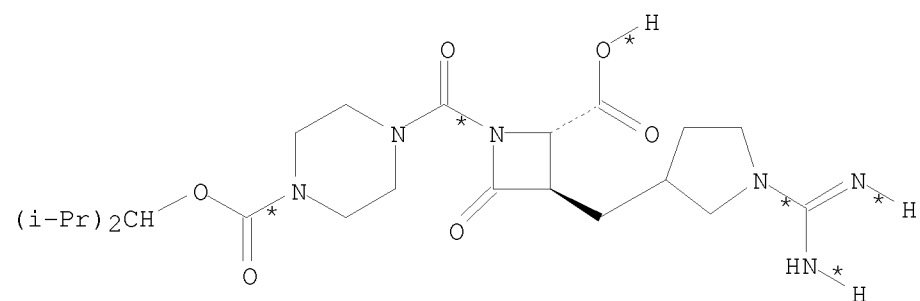
<12/04/2007>

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3
STEPS
→



RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

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RX(16) RCT AX 479622-21-4

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO BA 479622-23-6

NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)

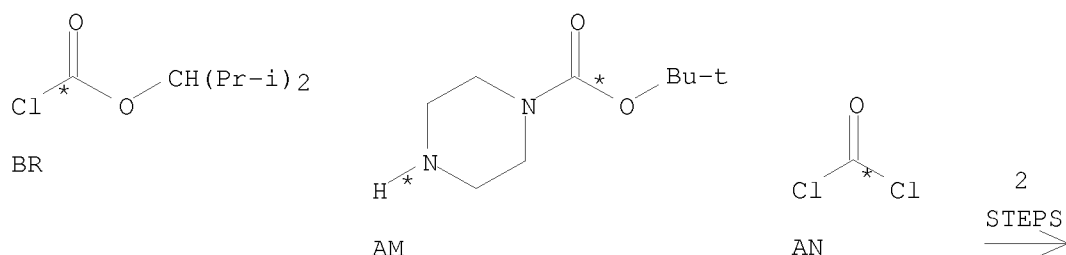
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

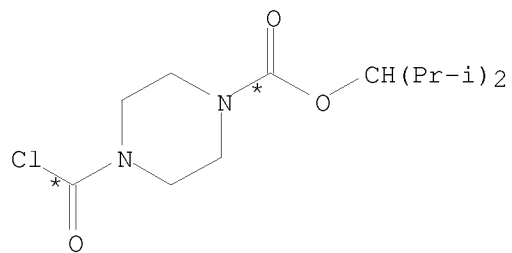
RX(133) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)
AND REACTION SEQUENCE RX(19), RX(5)

... BR + AM + AN ==> P...

...AZ + K + P ==> Y

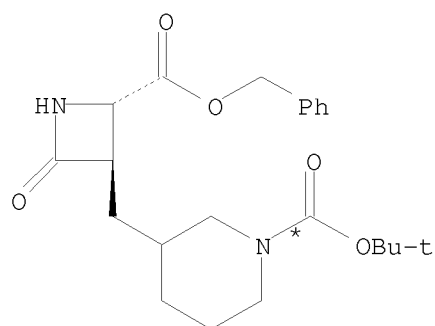


10/513699

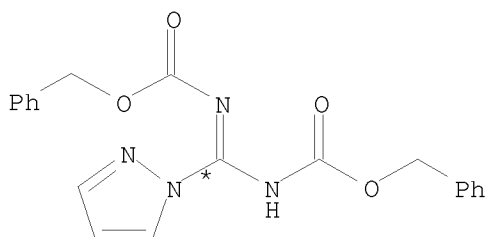


P

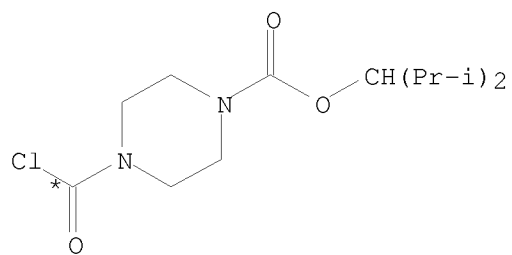
START NEXT REACTION SEQUENCE



AZ



K

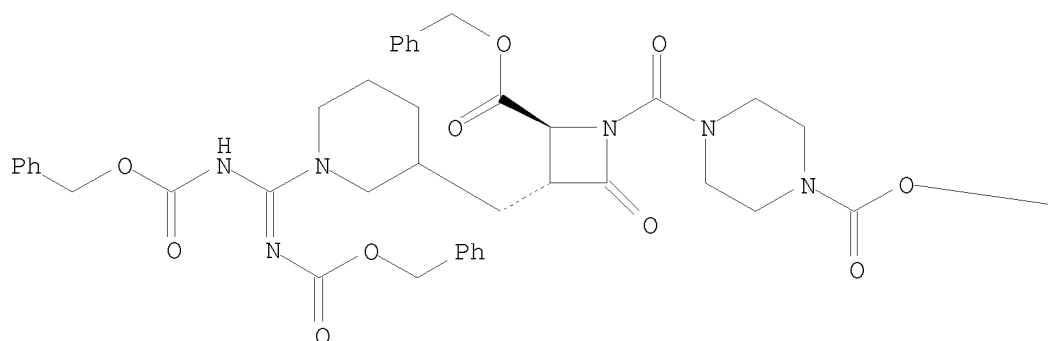


P

2
STEPS
→

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—CH(Pr-i)₂

Y
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F₃CCO₂H

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SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

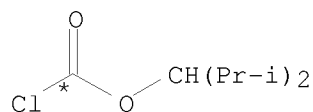
PRO X 384830-18-6
NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

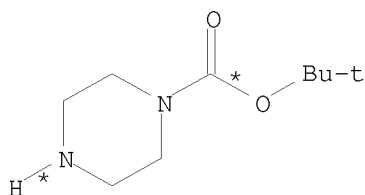
RX(134) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)
AND REACTION SEQUENCE RX(19), RX(21)

...4 BR + 4 AM + 4 AN ==> P...

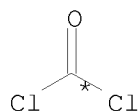
...4 AZ + 4 K + 4 P ==> BB + BC + BD + BE



4 BR

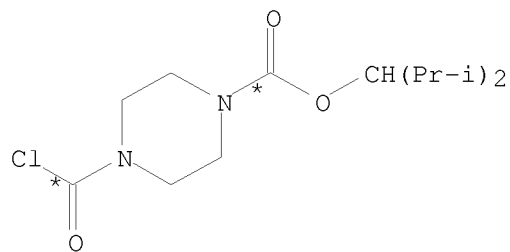


4 AM



4 AN

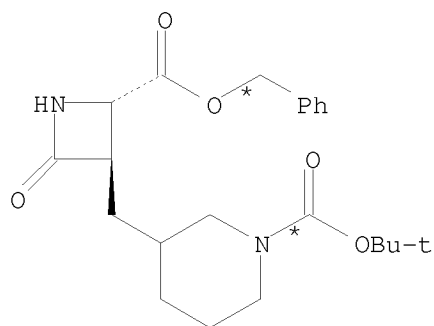
2
STEPS
→



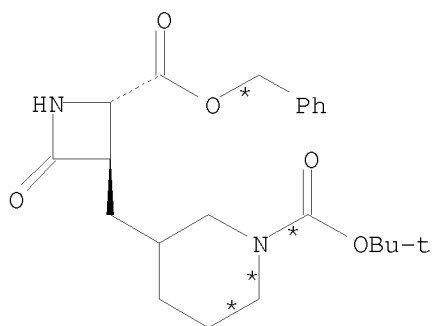
P

START NEXT REACTION SEQUENCE

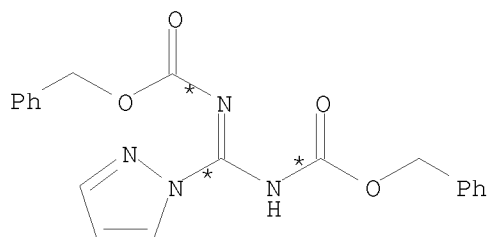
10/513699



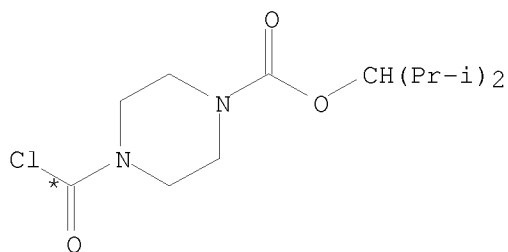
3 AZ



AZ

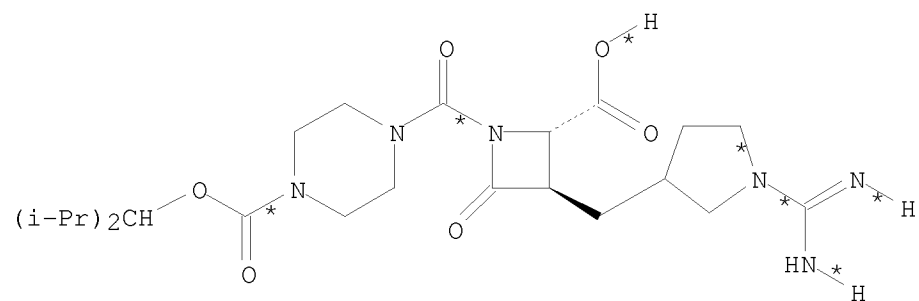


4 K



4 P

2
STEPS
→

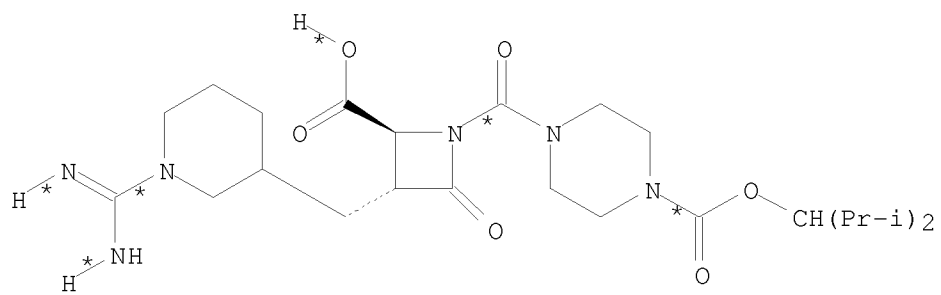


BB

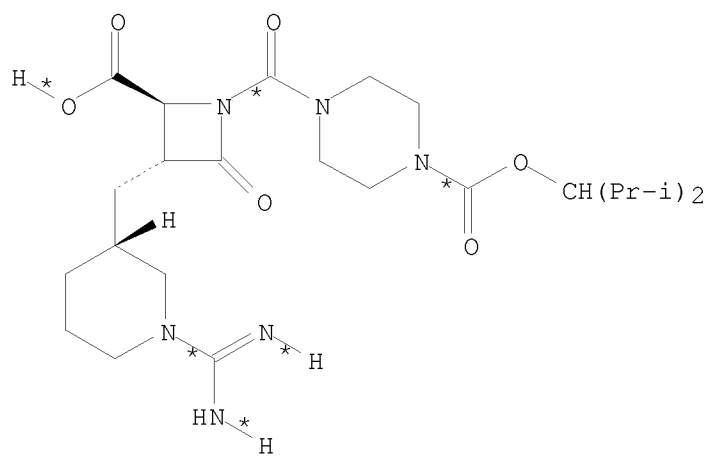
<12/04/2007>

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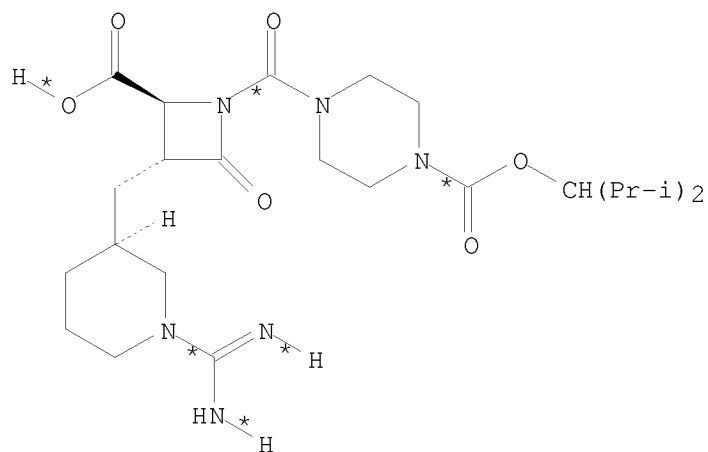


BC



BD

10/513699



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

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STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)

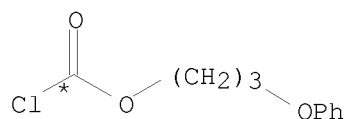
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE
479622-26-9

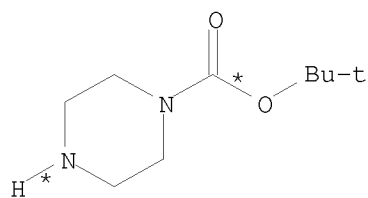
RX(138) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)
AND REACTION SEQUENCE RX(19), RX(25)

... BV + AM + AN ==> BK...

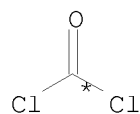
...AZ + K + BK ==> BL



BV



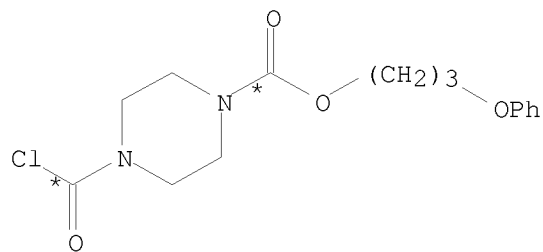
AM



AN

2

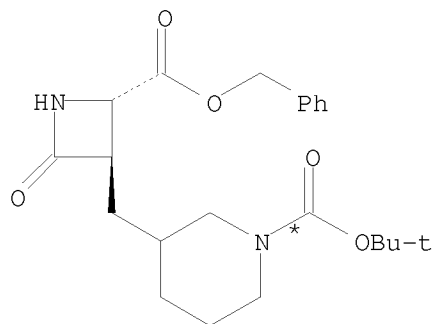
STEPS
→



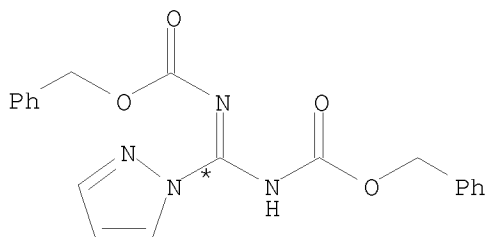
BK

START NEXT REACTION SEQUENCE

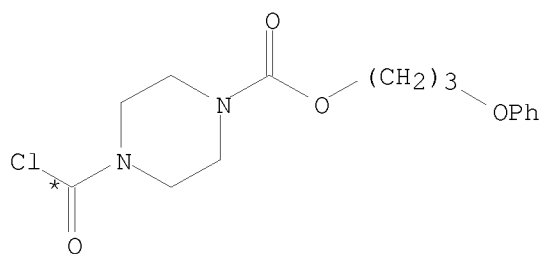
10/513699



AZ



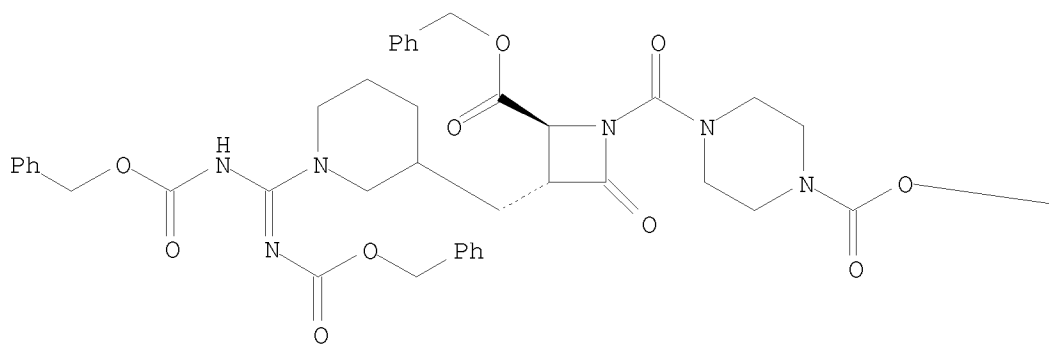
K



BK

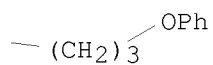
2
STEPS
→

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BL
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N

PRO BL 384830-26-6

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

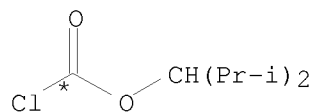
RX(146) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)

10/513699

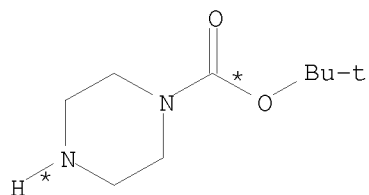
AND REACTION SEQUENCE RX(17), RX(19), RX(5)

... BR + AM + AN ==> P...

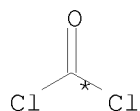
...AW + F + K + P ==> Y



BR

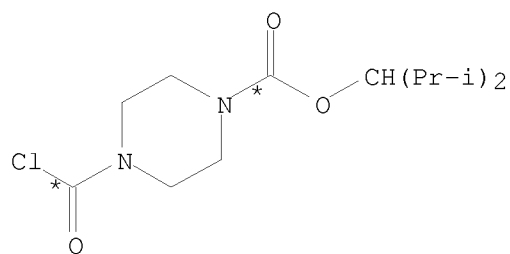


AM



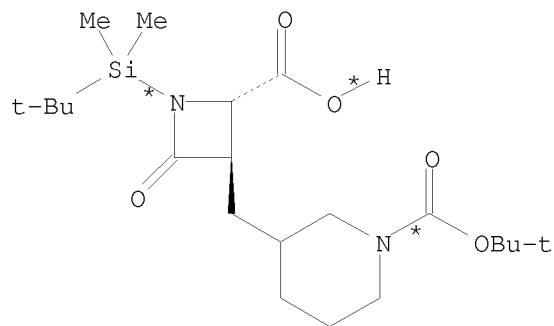
AN

3
STEPS
→

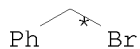


P

START NEXT REACTION SEQUENCE



AW

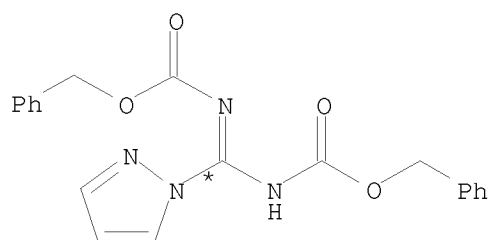


F

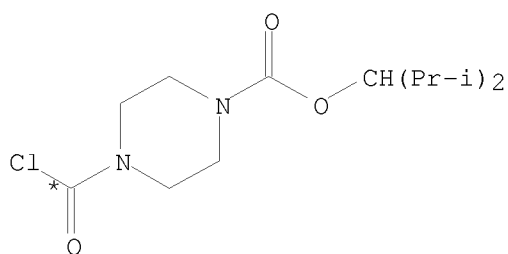
<12/04/2007>

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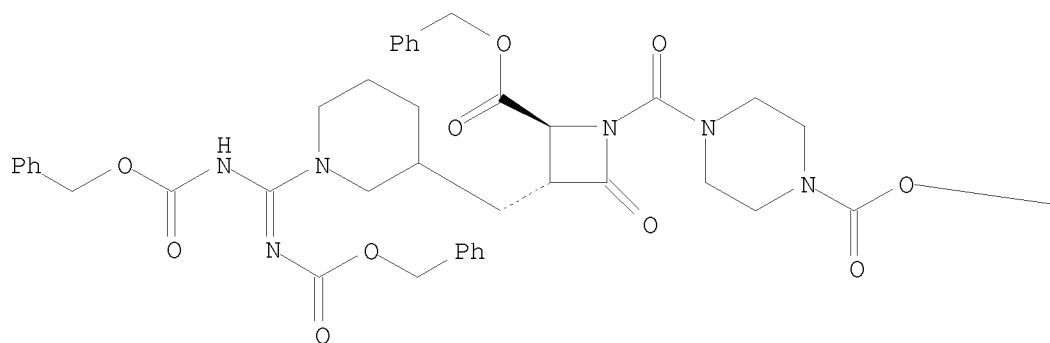
K



P

3
STEPS
→

PAGE 1-A



PAGE 1-B

—CH(Pr-i)₂

Y
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

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STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6

RGT N 121-44-8 Et3N

PRO Y 253177-10-5

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

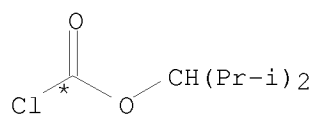
RX(147) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)

AND REACTION SEQUENCE RX(17), RX(19), RX(21)

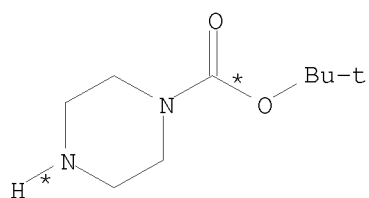
...4 BR + 4 AM + 4 AN ==> P...

...4 AW + 4 F + 4 K + 4 P ==> BB + BC + BD + BE

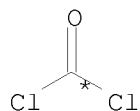
10/513699



4 BR

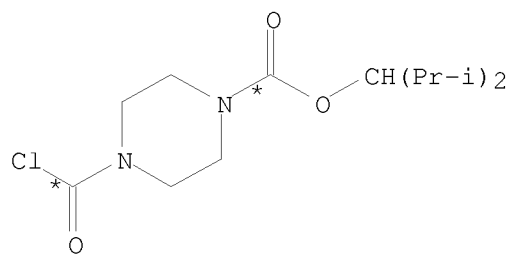


4 AM



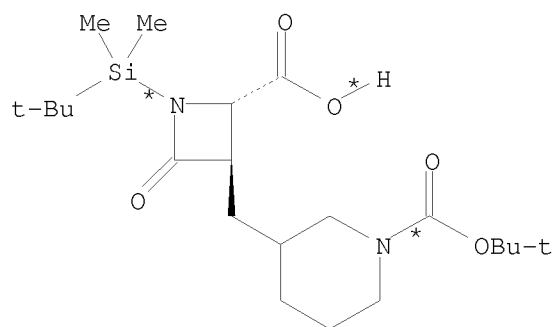
4 AN

3
STEPS
→



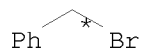
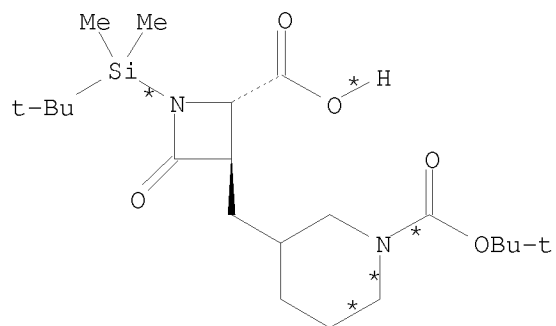
P

START NEXT REACTION SEQUENCE



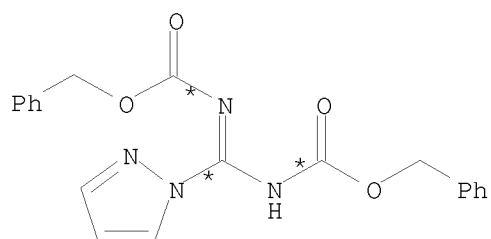
3 AW

10/513699

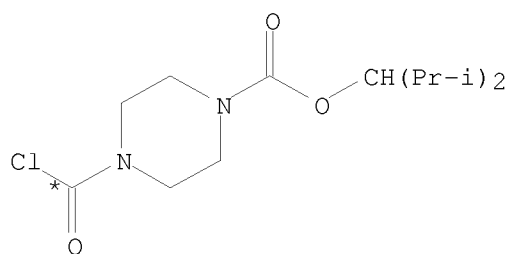


AW

4 F

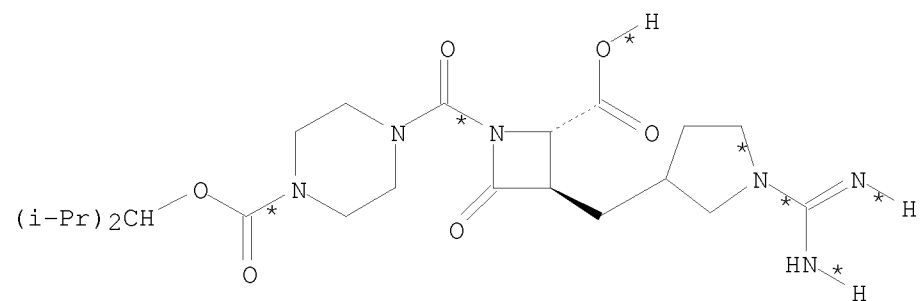


4 K



4 P

3
STEPS
→

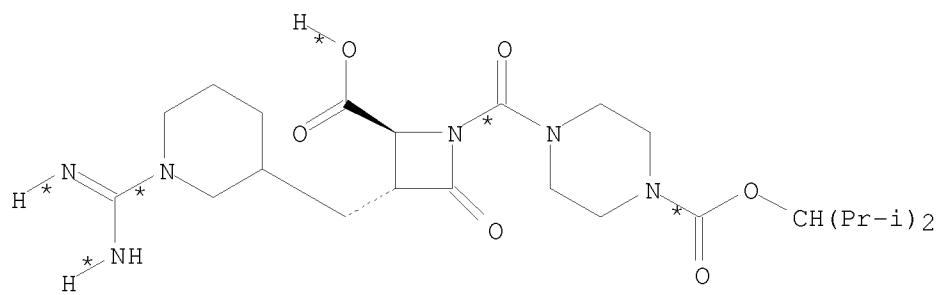


BB

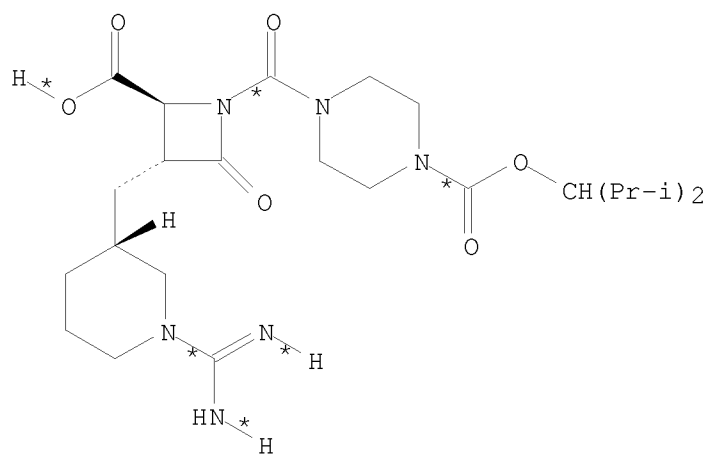
<12/04/2007>

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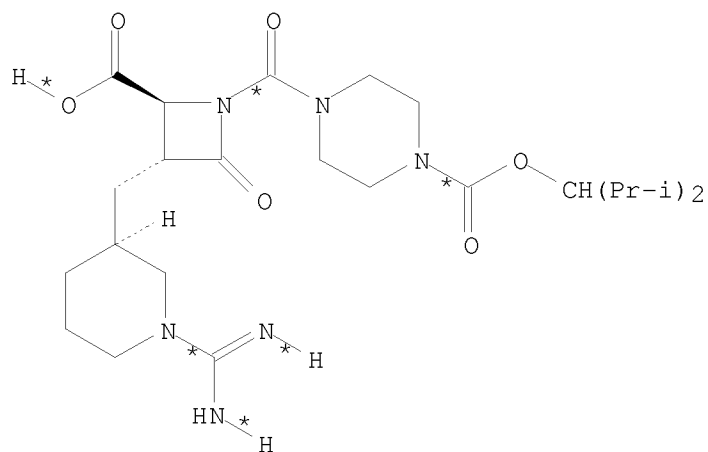


BC



BD

10/513699



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu₄N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO₃

SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

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RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

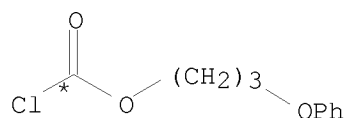
STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

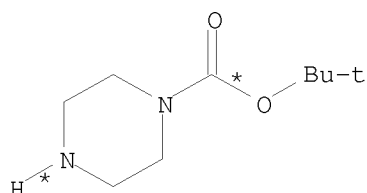
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE
479622-26-9

RX(151) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)
AND REACTION SEQUENCE RX(17), RX(19), RX(25)

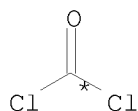
... BV + AM + AN ==> BK...
...AW + F + K + BK ==> BL



BV



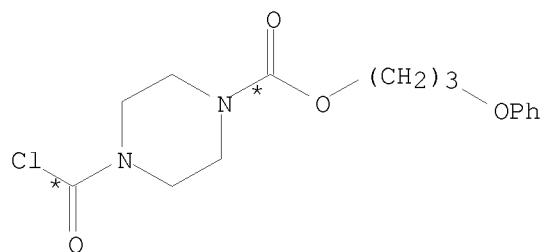
AM



AN

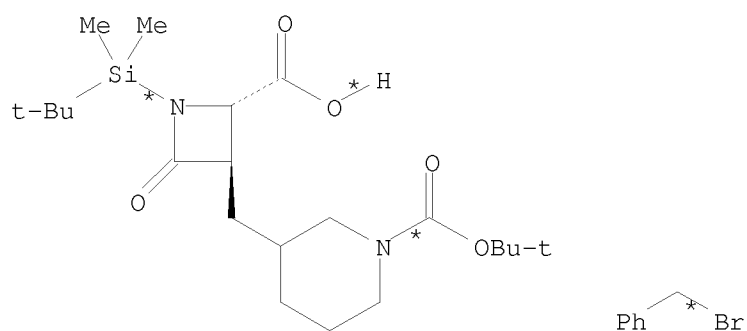
3
STEPS
→

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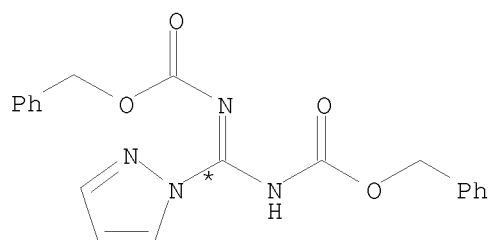
BK

START NEXT REACTION SEQUENCE

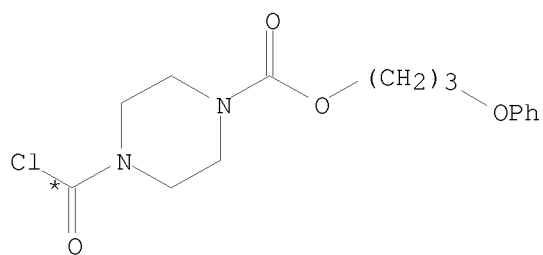


AW

F



K

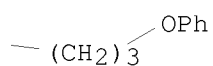
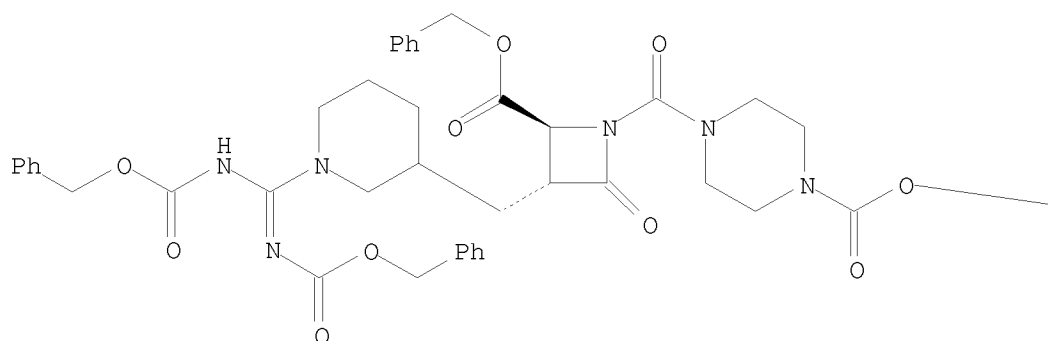


BK

3
STEPS
→

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BL
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F

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SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

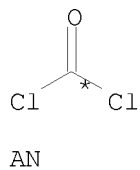
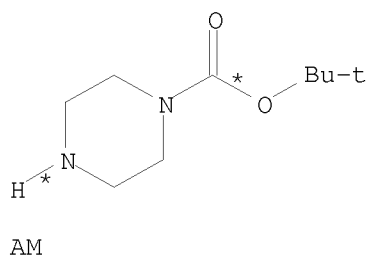
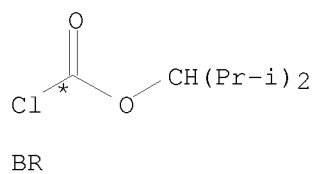
STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

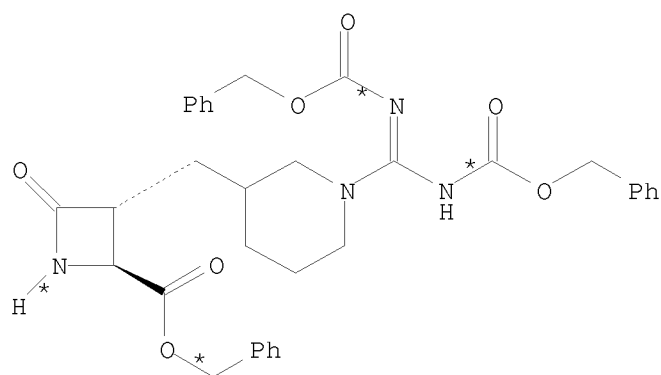
PRO X 384830-18-6
NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et3N
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(155) OF 275 COMPOSED OF RX(29), RX(5), RX(44)
RX(155) BR + AM + AN + X ==> BC

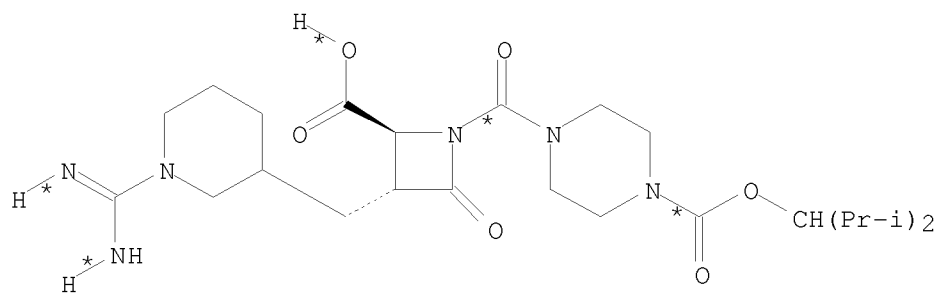


10/513699



X

3
STEPS
→



BC
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N

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PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RG T S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

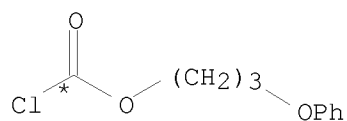
SOL 7732-18-5 Water

PRO BC 253177-54-7

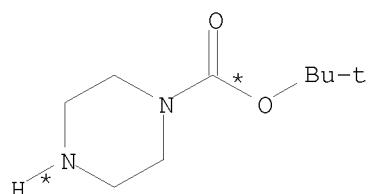
NTE polyvinylpyridine resin used in second stage

RX(160) OF 275 COMPOSED OF RX(33), RX(25), RX(37)

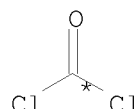
RX(160) BV + AM + AN + X ==> BZ



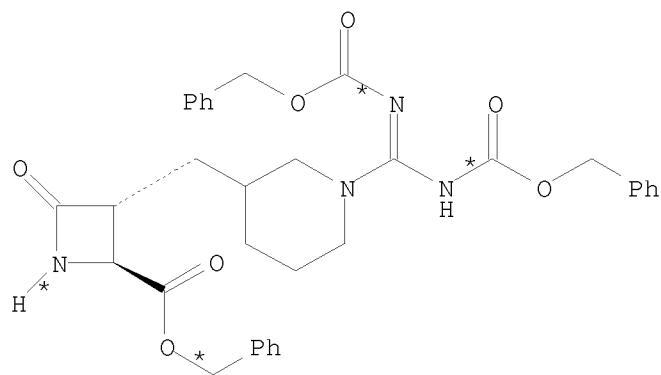
BV



AM



AN



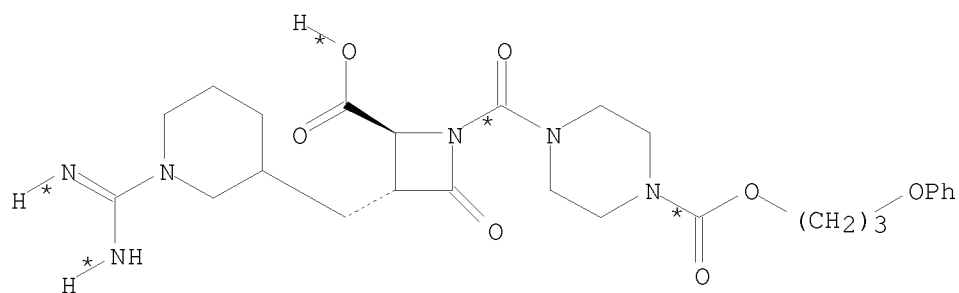
X

3
STEPS
→

<12/04/2007>

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BZ
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N

PRO BL 384830-26-6

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

RX(168) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)

<12/04/2007>

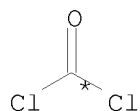
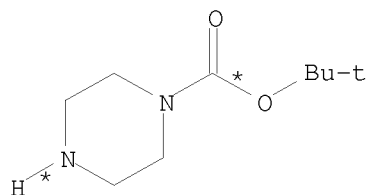
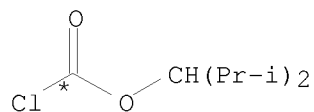
Erich Leese

10/513699

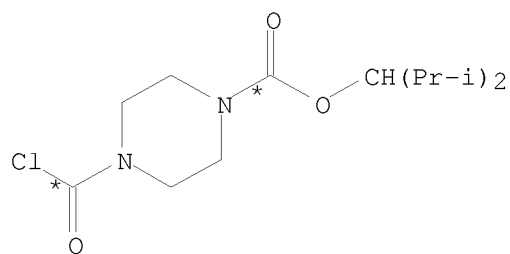
AND REACTION SEQUENCE RX(1), RX(2), RX(3), RX(4)

... BR + AM + AN ==> P...

...A + B + F + K + P ==> Q

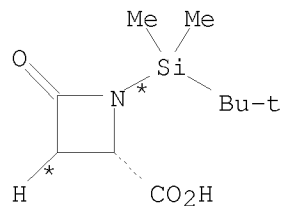
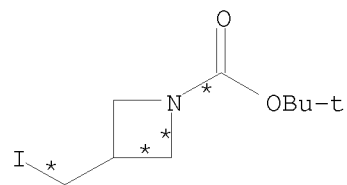


4
STEPS
→



P

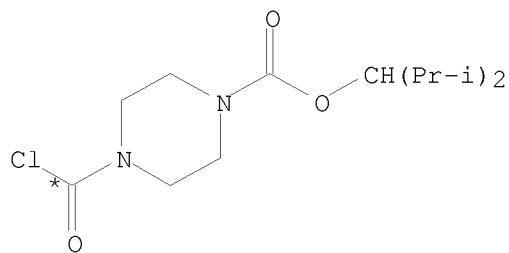
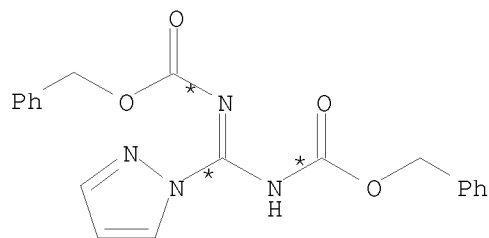
START NEXT REACTION SEQUENCE



A

B

F



K

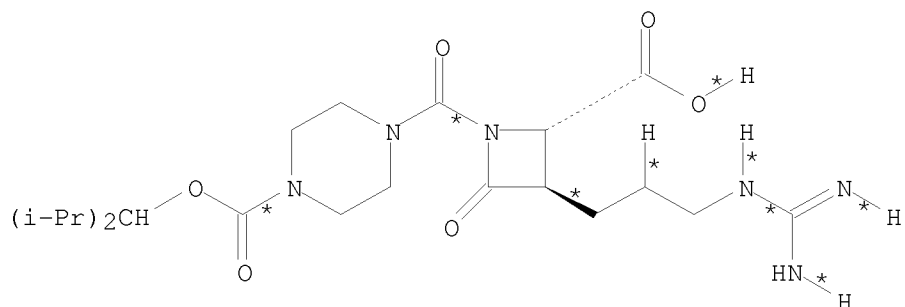
P

<12/04/2007>

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10/513699

4
STEPS
→



Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(1) RCT A 253176-94-2, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)₂

PRO C 253176-95-3

SOL 109-99-9 THF

NTE stereoselective

RX(2) RCT C 253176-95-3

STAGE(1)

RGT H 429-41-4 Bu₄N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

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RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO G 253176-97-5

RX(3) RCT G 253176-97-5

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO L 253177-00-3
NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

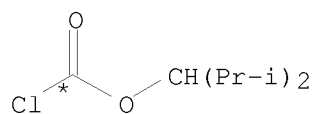
STAGE(1)
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

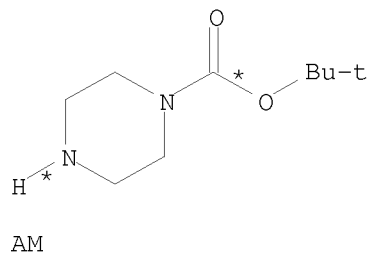
PRO Q 253173-70-5

RX(170) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)
AND REACTION SEQUENCE RX(6), RX(1), RX(2), RX(3), RX(4)

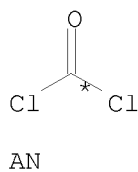
... BR + AM + AN ==> P...
...Z + B + F + K + P ==> Q



BR



AM



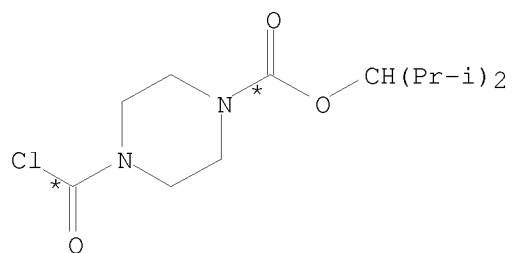
AN

5
STEPS
→

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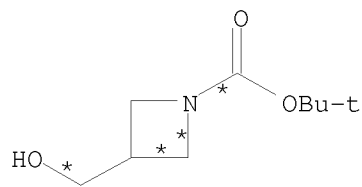
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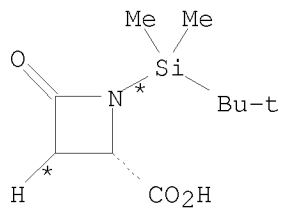


P

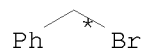
START NEXT REACTION SEQUENCE



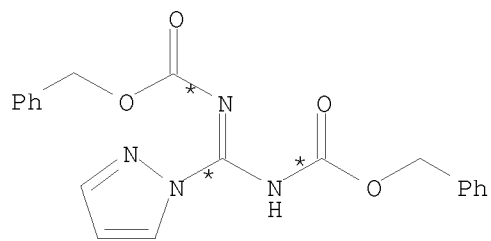
Z



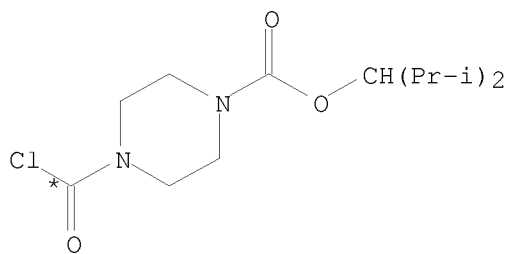
B



F



K



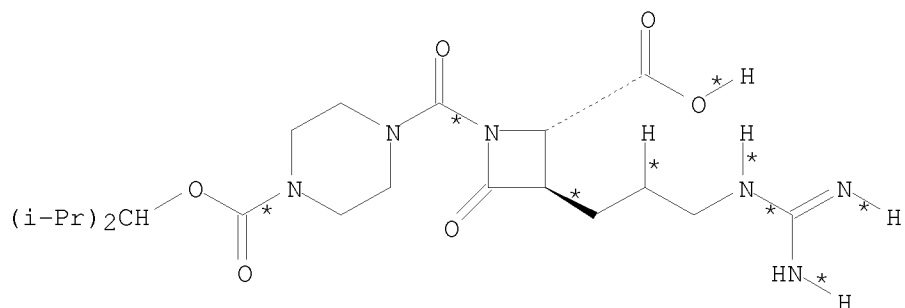
P

5
STEPS
→

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Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(6) RCT Z 142253-56-3

RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole

PRO A 253176-94-2

SOL 75-09-2 CH₂Cl₂

RX(1) RCT A 253176-94-2, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)₂

PRO C 253176-95-3

SOL 109-99-9 THF

NTE stereoselective

RX(2) RCT C 253176-95-3

STAGE(1)

RGT H 429-41-4 Bu₄N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO₃

SOL 68-12-2 DMF

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PRO G 253176-97-5

RX(3) RCT G 253176-97-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO L 253177-00-3

NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

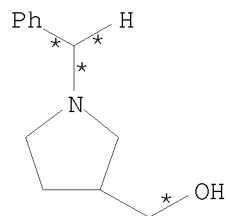
CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

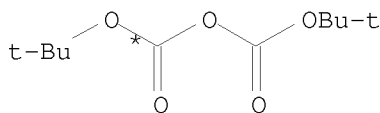
PRO Q 253173-70-5

RX(171) OF 275 COMPOSED OF RX(7), RX(8), RX(43), RX(16), RX(18)

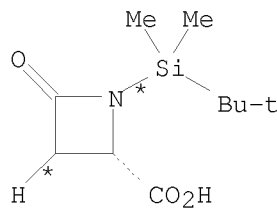
RX(171) AD + AE + B + F + K ==> BA



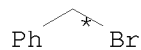
AD



AE



B

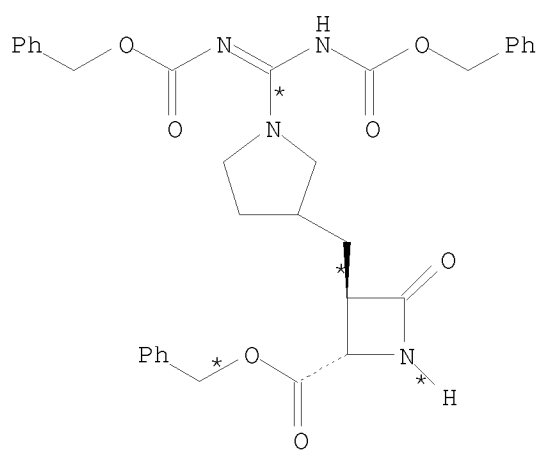
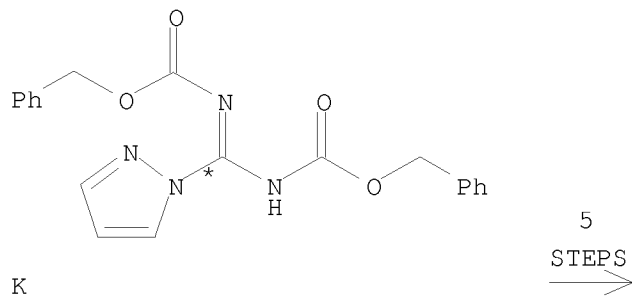


F

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BA

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5
SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AH 479622-36-1
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9

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RGT D 4111-54-0 LiN(Pr-i)2
PRO AX 479622-21-4
SOL 109-99-9 THF
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)
RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AY 479622-22-5

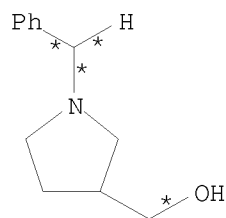
RX(18) RCT AY 479622-22-5

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

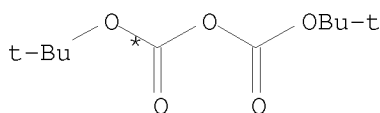
STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO BA 479622-23-6
NTE alternative prepn. shown

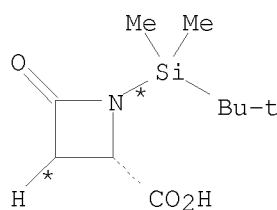
RX(173) OF 275 COMPOSED OF RX(7), RX(8), RX(43), RX(16), RX(18), RX(20)
RX(173) AD + AE + B + F + K + P ==> BB



AD

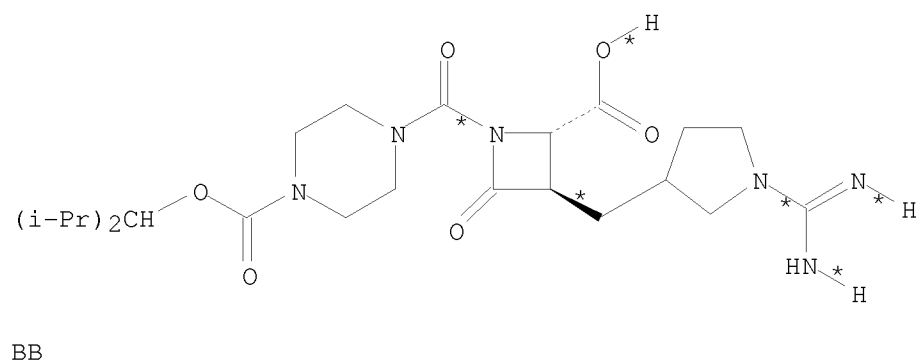
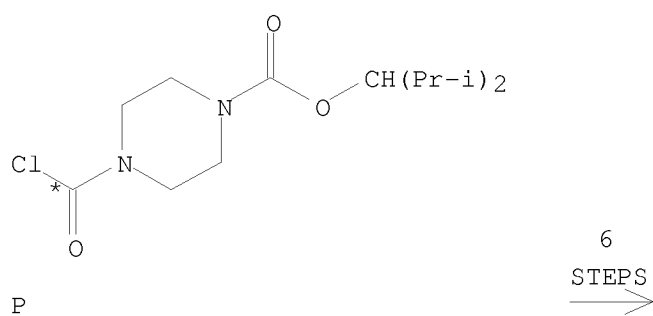
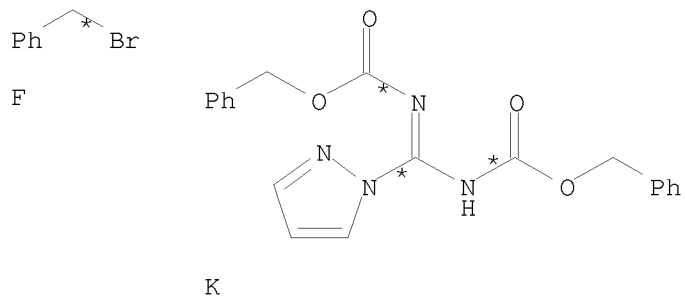


AE



B

10/513699



RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5
SOL 109-99-9 THF

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PRO AF 114214-69-6
NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AH 479622-36-1
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AX 479622-21-4
SOL 109-99-9 THF
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO BA 479622-23-6
NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

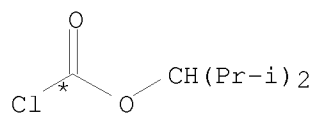
RX(201) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)

10/513699

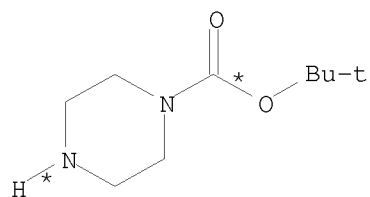
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(5)

... BR + AM + AN ==> P...

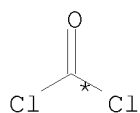
...AL + B + F + K + P ==> Y



BR

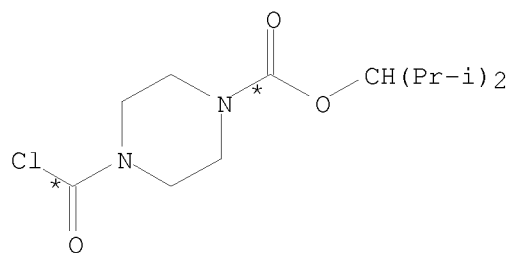


AM



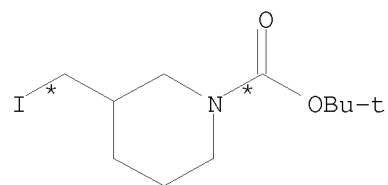
AN

4
STEPS
➔

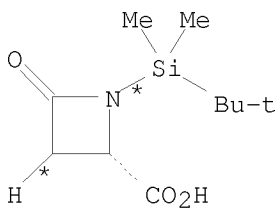


P

START NEXT REACTION SEQUENCE



AL



B

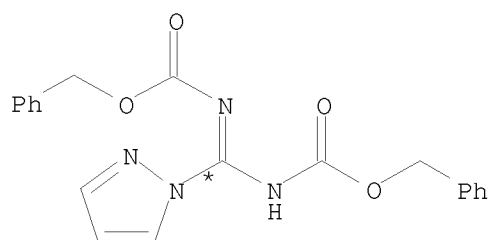


F

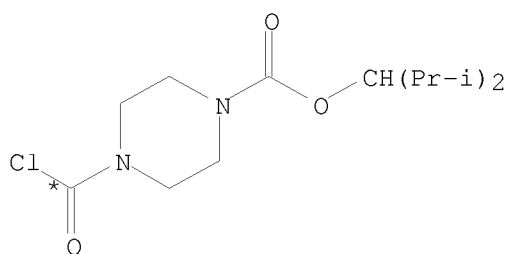
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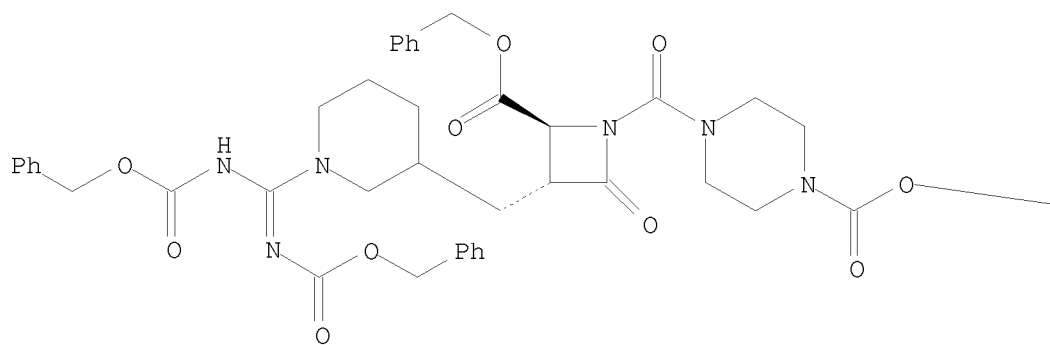
K



P

4
STEPS
→

PAGE 1-A



PAGE 1-B

—CH(Pr-i)₂

Y
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

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STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)₂
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu₄N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO₃
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

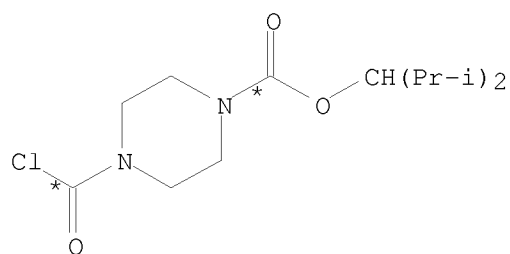
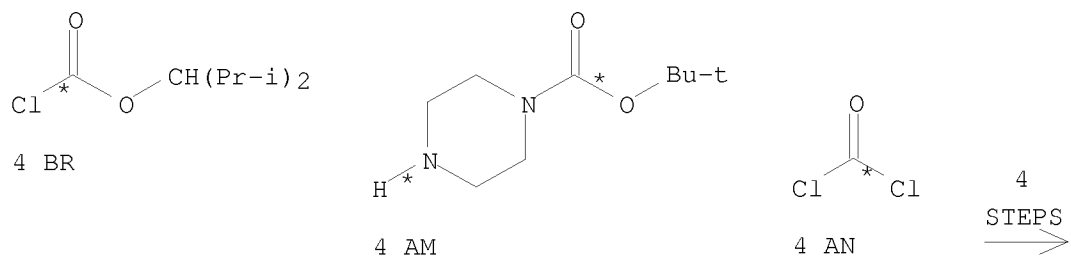
PRO X 384830-18-6

NTE alternative prep. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et₃N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

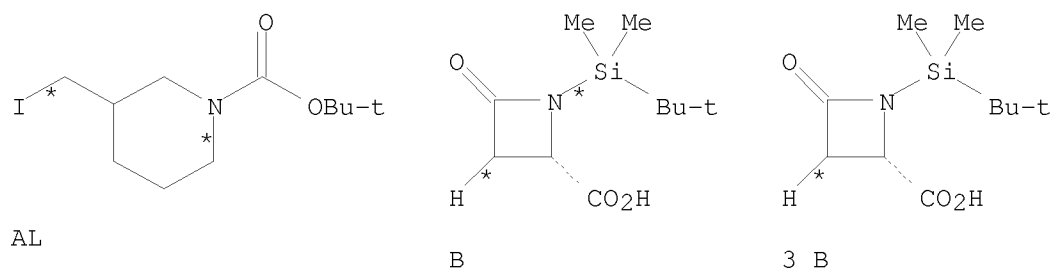
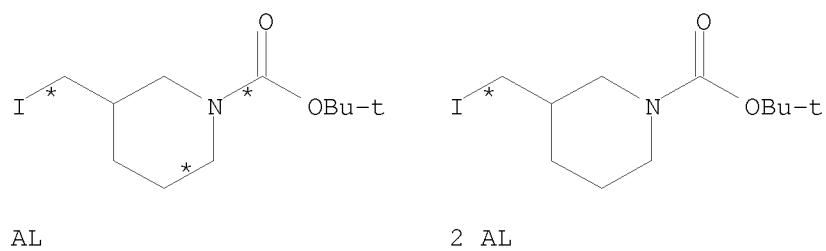
10/513699

RX(202) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(21)
...4 BR + 4 AM + 4 AN ==> P...
...4 AL + 4 B + 4 F + 4 K + 4 P ==> BB + BC + BD +
BE



P

START NEXT REACTION SEQUENCE



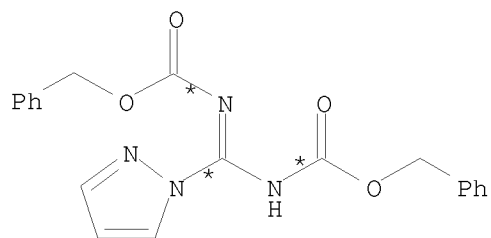
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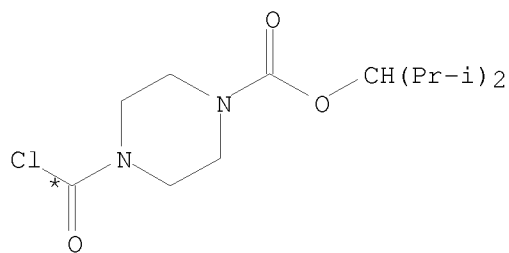
10/513699



4 F

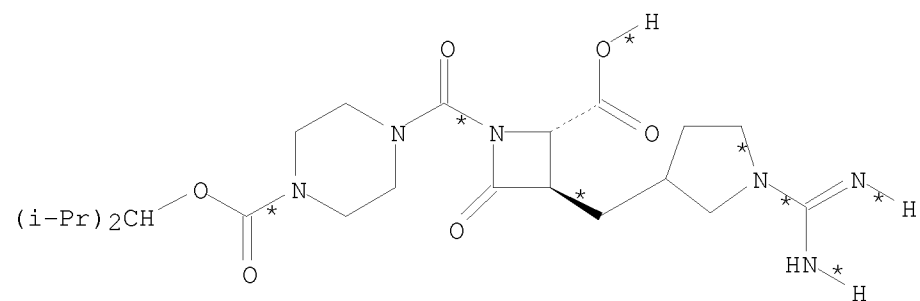


4 K

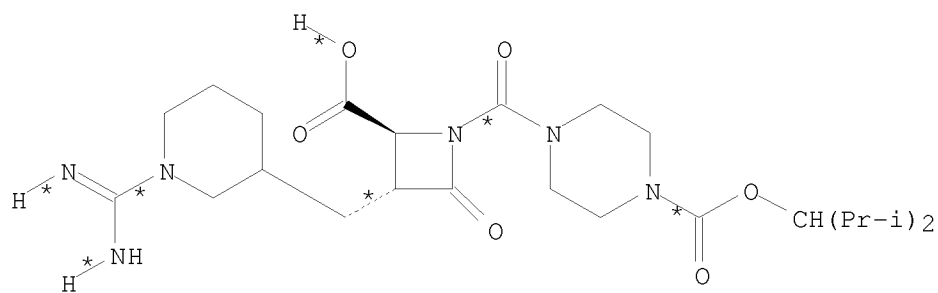


4 P

4
STEPS
→



BB

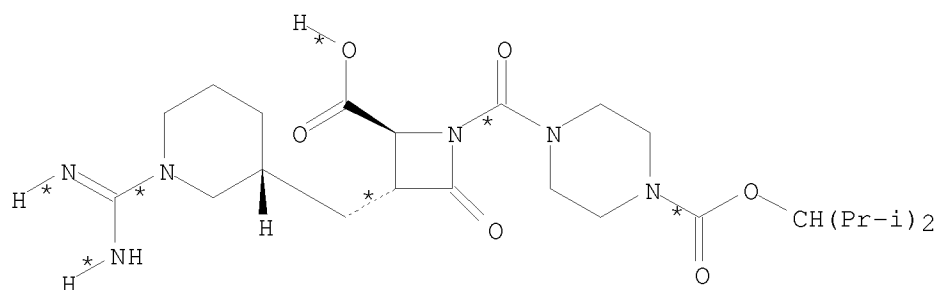


BC

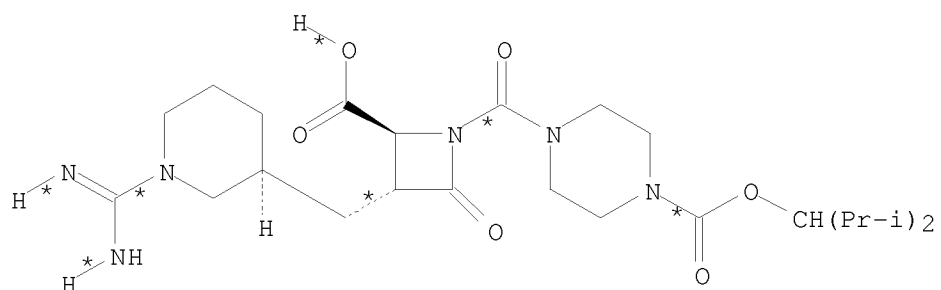
<12/04/2007>

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BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)₂

PRO AW 253177-04-7

SOL 109-99-9 THF

NTE stereoselective

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RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

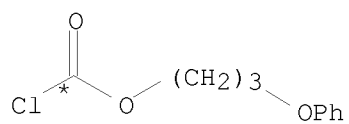
STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

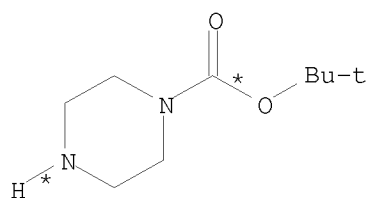
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE
479622-26-9

RX(206) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(25)
... BV + AM + AN ==> BK...
...AL + B + F + K + BK ==> BL

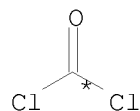
10/513699



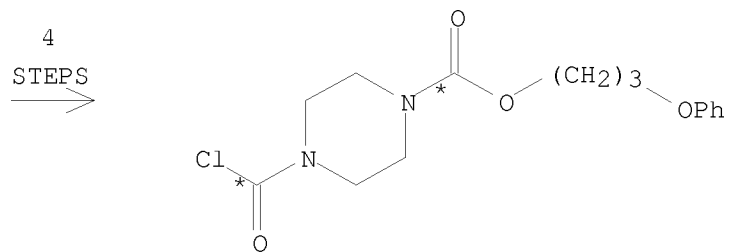
BV



AM

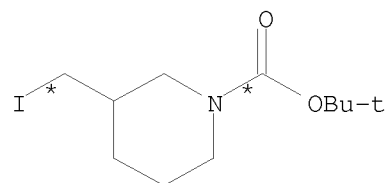


AN

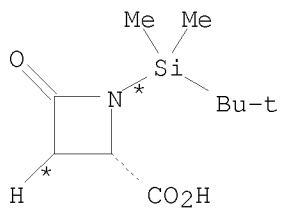


BK

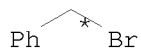
START NEXT REACTION SEQUENCE



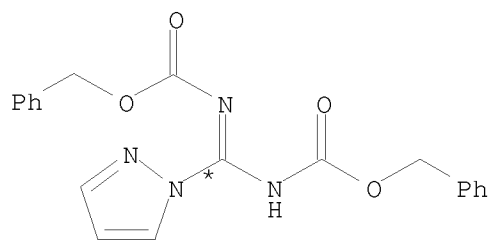
AL



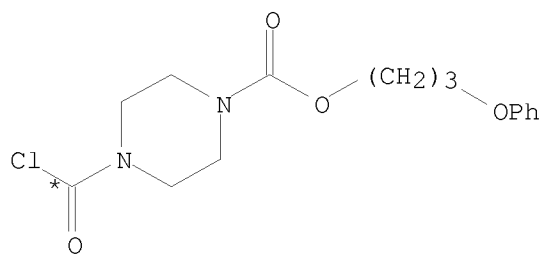
B



F



K



BK

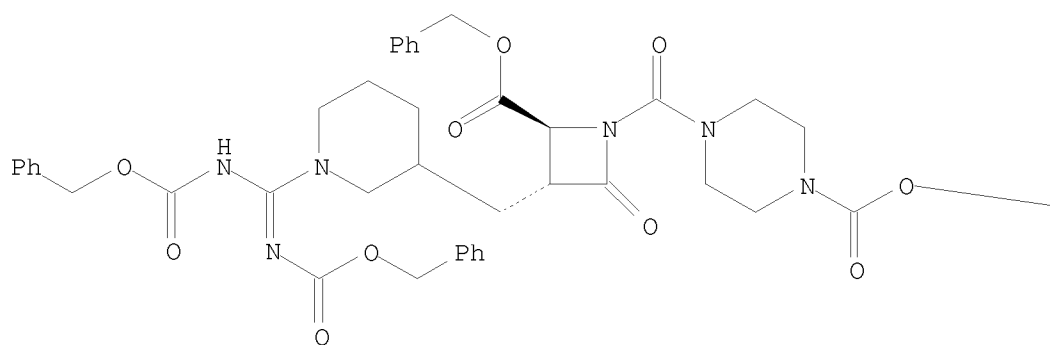
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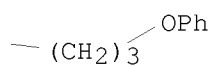
10/513699

4
STEPS
→

PAGE 1-A



PAGE 1-B



BL
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative

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prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

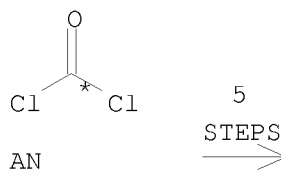
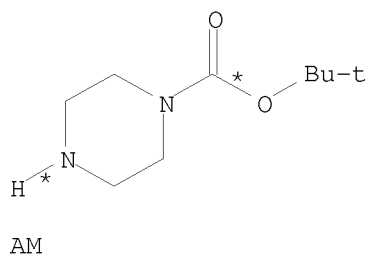
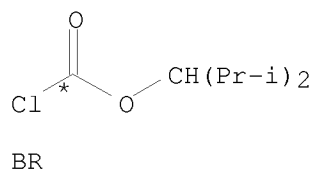
NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et3N
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(214) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(5)

... BR + AM + AN ==> P...

...AJ + B + F + K + P ==> Y

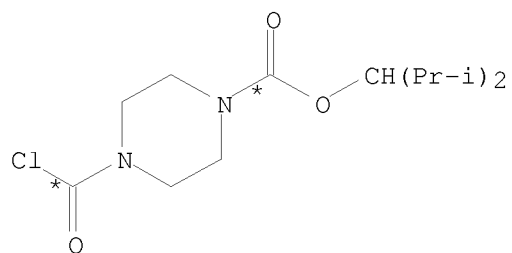


5
STEPS
→

<12/04/2007>

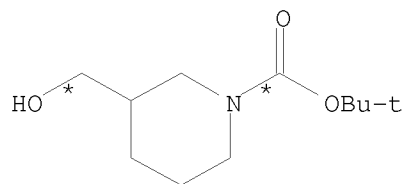
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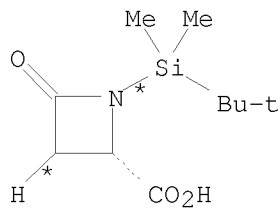


P

START NEXT REACTION SEQUENCE



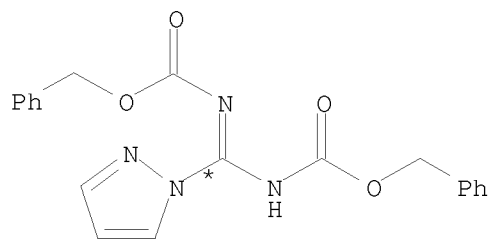
AJ



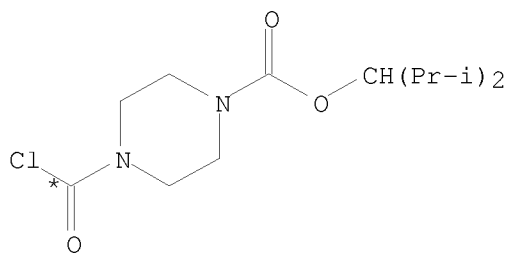
B



F



K

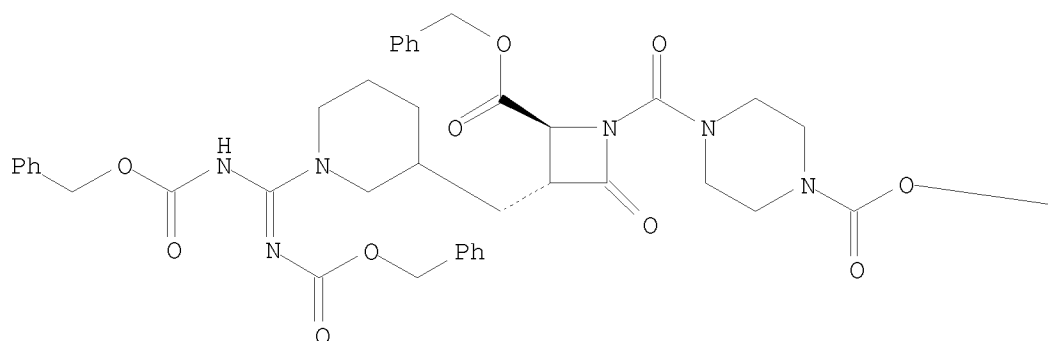


P

5
STEPS
→

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—CH(Pr-i)₂

Y
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH₂Cl₂

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RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

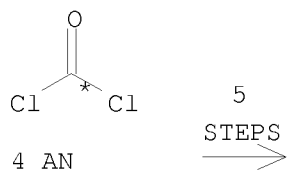
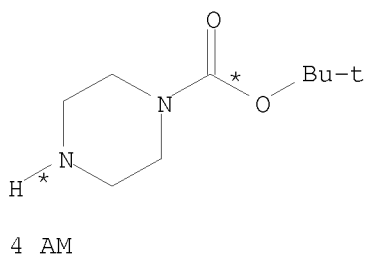
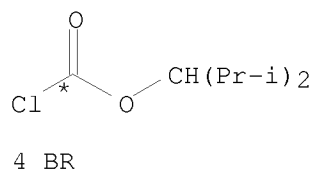
PRO X 384830-18-6

NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

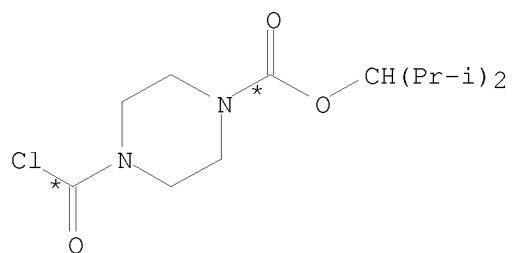
RX(215) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(21)

...4 BR + 4 AM + 4 AN ==> P...
...4 AJ + 4 B + 4 F + 4 K + 4 P ==> BB + BC + BD +
BE



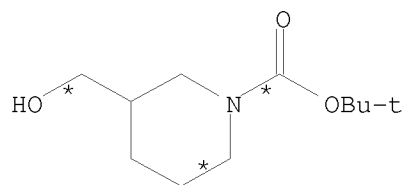
5
STEPS
→

10/513699

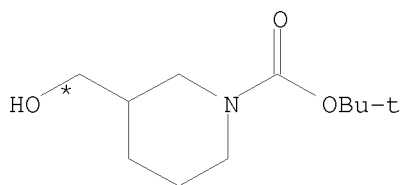


P

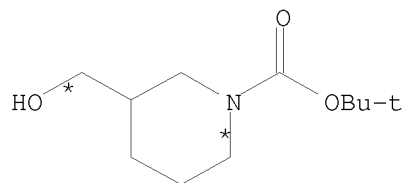
START NEXT REACTION SEQUENCE



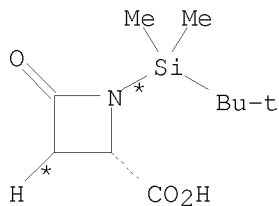
AJ



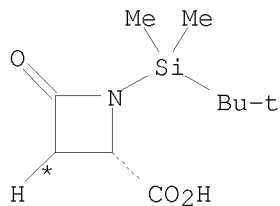
2 AJ



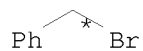
AJ



B



3 B

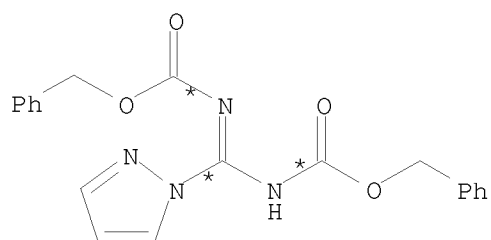


4 F

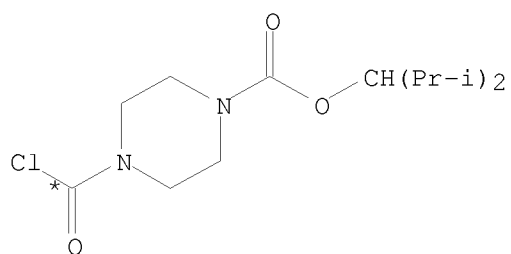
<12/04/2007>

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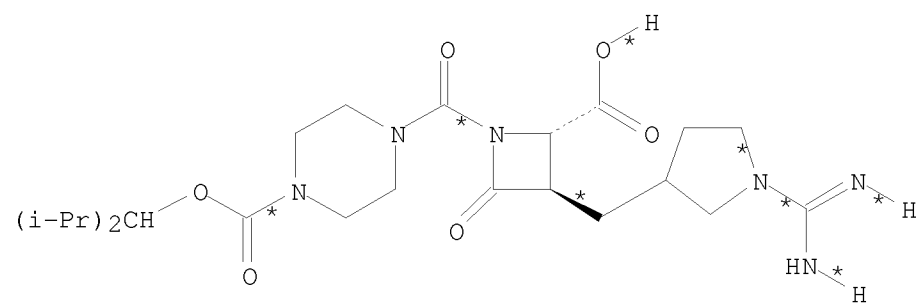


4 K

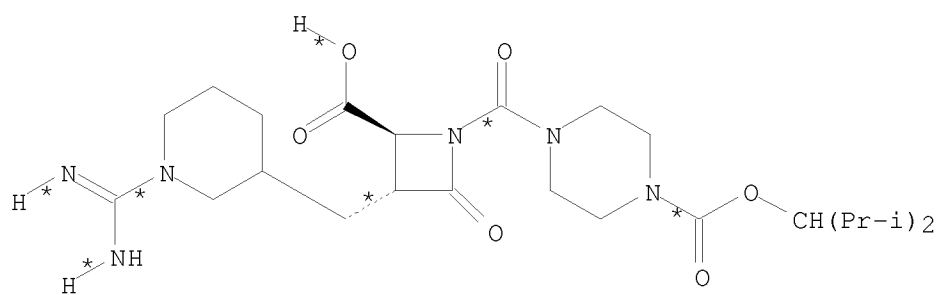


4 P

5
STEPS
→



BB

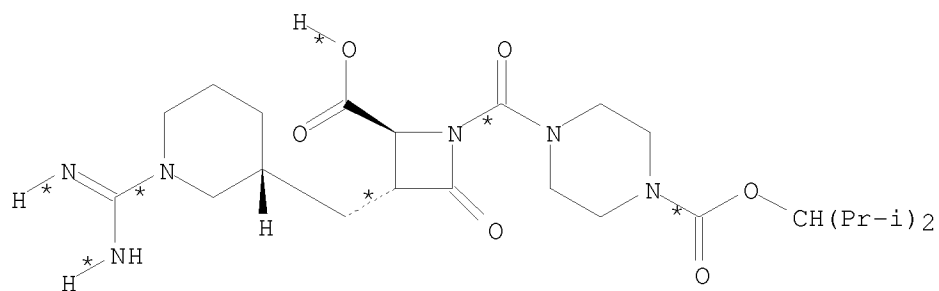


BC

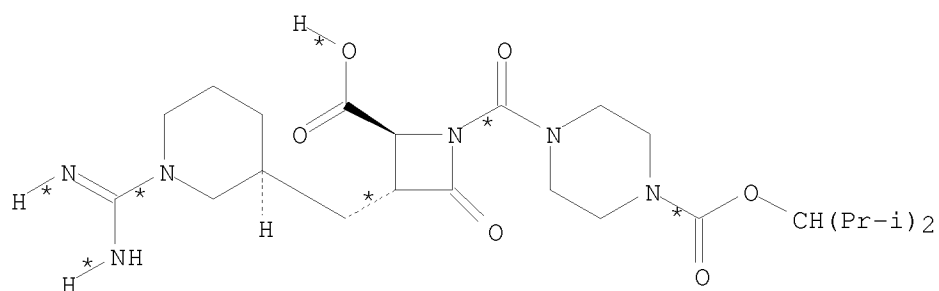
<12/04/2007>

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BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH₂Cl₂

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)₂

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PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)
RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

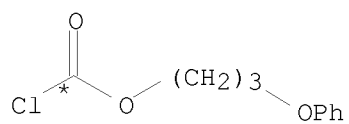
STAGE(1)
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

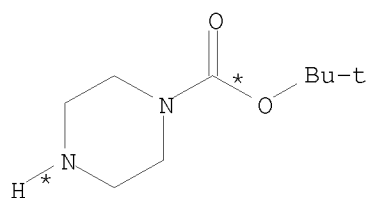
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE
479622-26-9

RX(219) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(25)
... BV + AM + AN ==> BK...
...AJ + B + F + K + BK ==> BL

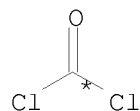
10/513699



BV

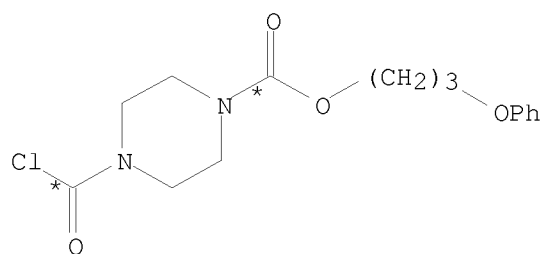


AM



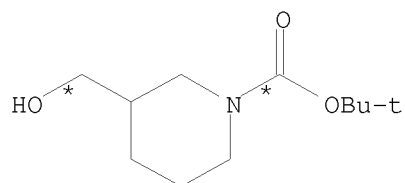
AN

5
STEPS
→

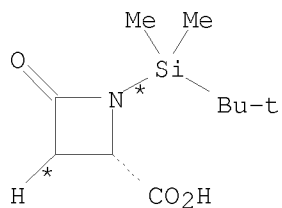


BK

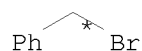
START NEXT REACTION SEQUENCE



AJ

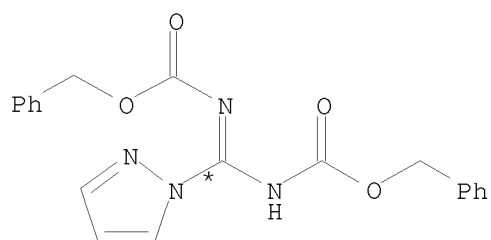


B

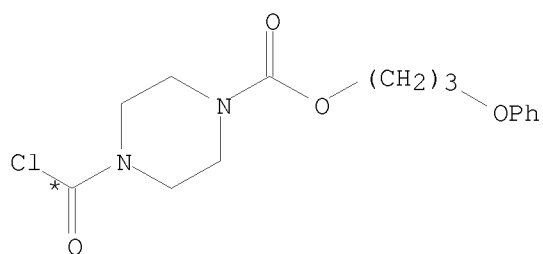


F

10/513699



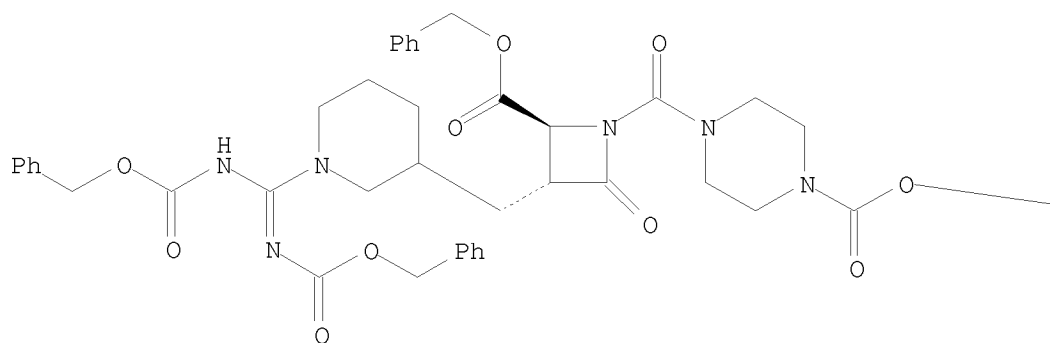
K



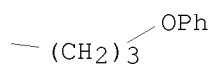
BK

5
STEPS
→

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PAGE 1-B



BL
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

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STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH₂Cl₂

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)₂
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu₄N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO₃
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et₃N

<12/04/2007>

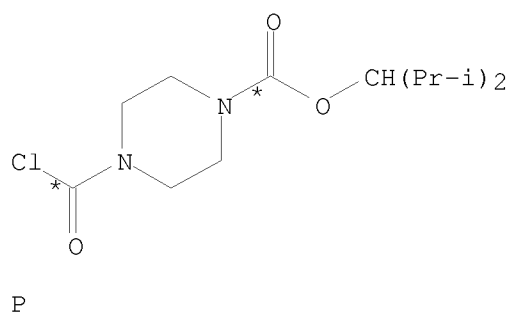
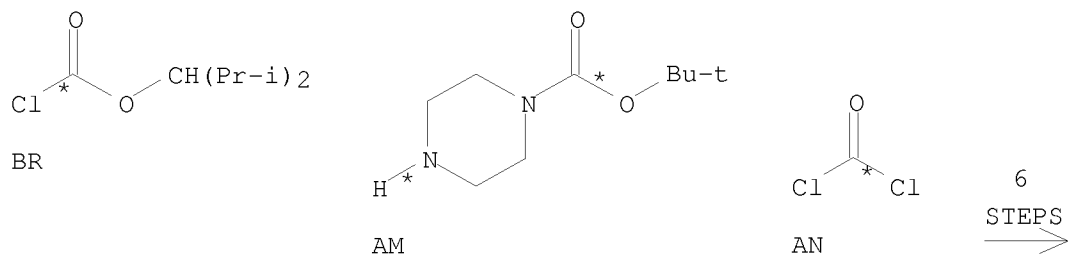
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10/513699

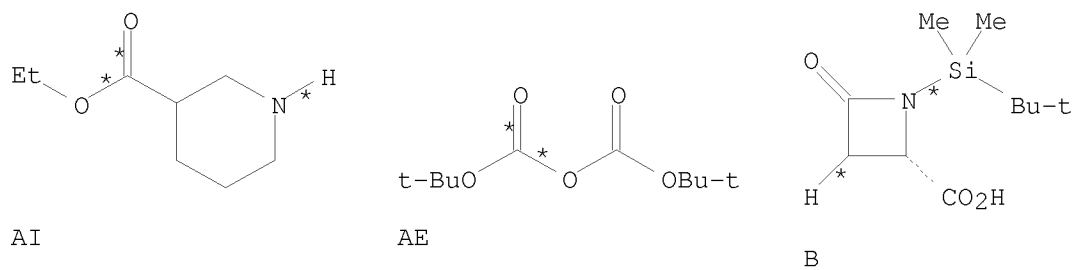
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(227) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),
RX(5)

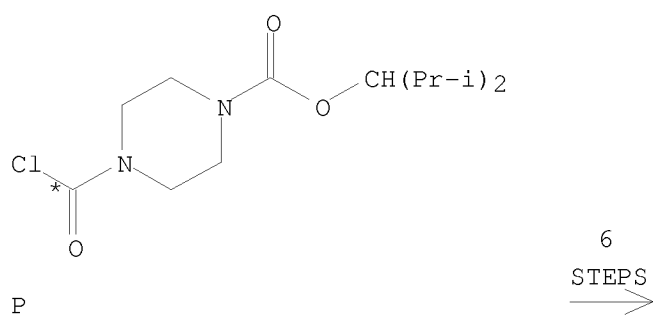
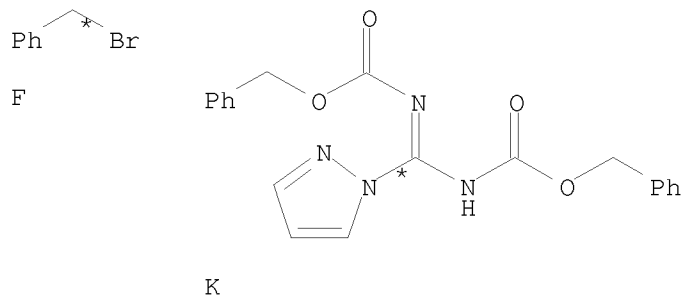
... BR + AM + AN ==> P...
...AI + AE + B + F + K + P ==> Y



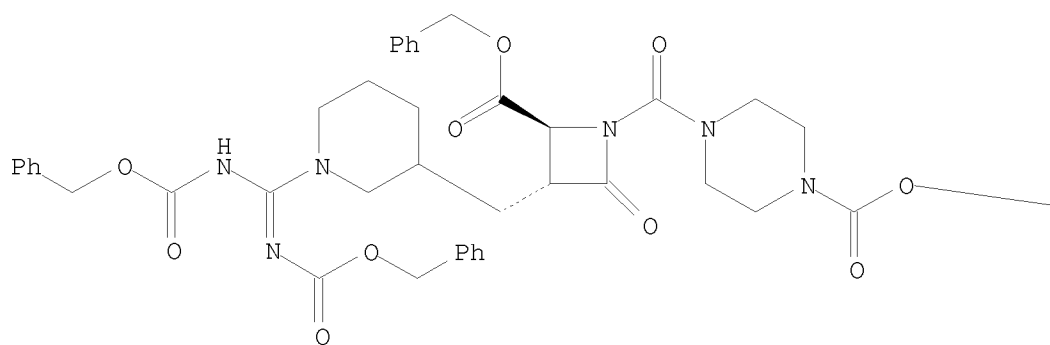
START NEXT REACTION SEQUENCE



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$\text{CH}(\text{Pr-i})_2$

Y
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH4
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

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RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6

RGT N 121-44-8 Et3N

PRO Y 253177-10-5

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

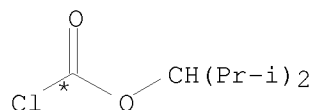
RX(228) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)

AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),

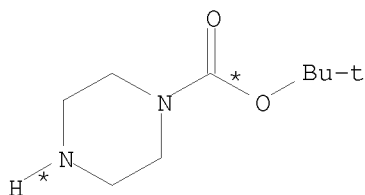
RX(21)

...4 BR + 4 AM + 4 AN ==> P...

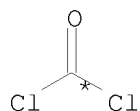
...4 AI + 4 AE + 4 B + 4 F + 4 K + 4 P ==> BB + BC +
BD + BE



4 BR



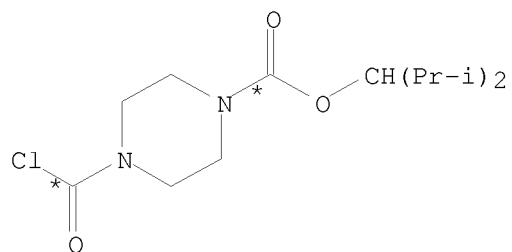
4 AM



4 AN

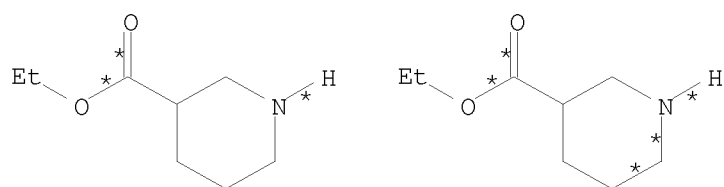
6
STEPS
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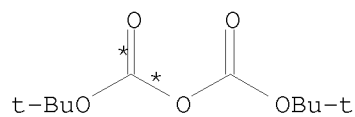
P

START NEXT REACTION SEQUENCE

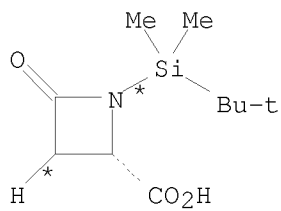


3 AI

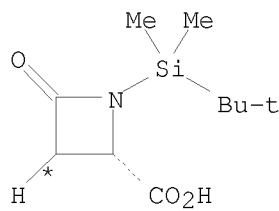
AI



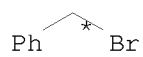
4 AE



B

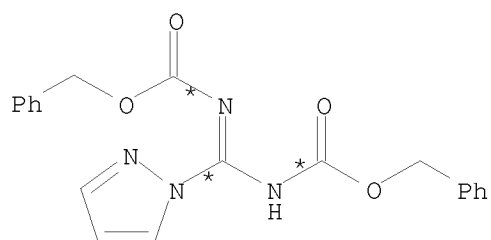


3 B

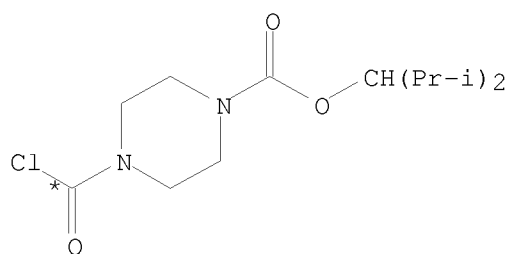


4 F

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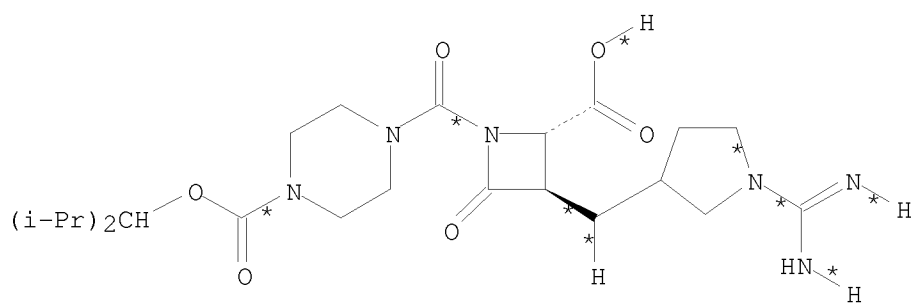


4 K

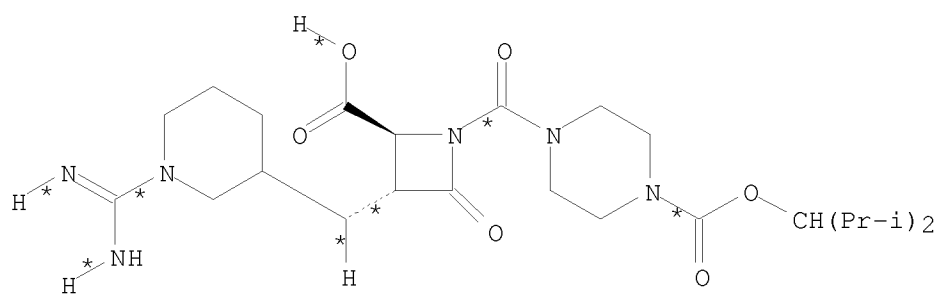


4 P

6
STEPS
→



BB



BC

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[illegible]

The chemical structure of compound 6 consists of a central piperidine ring. The nitrogen of the piperidine is substituted with a guanidino group ($\text{N}=\text{C}(\text{NH}_2)\text{NH}_2$). One carbon of the piperidine ring is substituted with a hydrogen atom (H) and a side chain. The side chain begins with a methylene group (CH_2) connected to a four-membered ring containing one nitrogen and two carbonyl groups ($\text{O}=\text{C}-\text{N}-\text{C}(=\text{O})$). This four-membered ring is further substituted with a carbamate group ($\text{N}(\text{CH}_2)_2\text{C}(=\text{O})\text{OCH}_2\text{CH}(\text{Pr-i})_2$). Stereochemistry is indicated by dashed bonds for the hydrogen at C-2 and the side chain attachment point.

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SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)
RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE
479622-26-9

<12/04/2007>

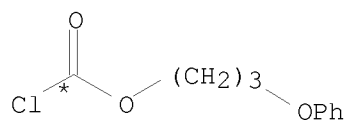
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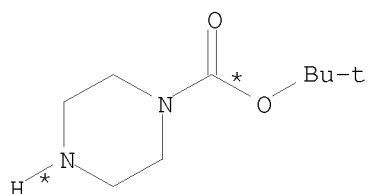
RX(232) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),
RX(25)

... BV + AM + AN ==> BK...

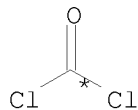
...AI + AE + B + F + K + BK ==> BL



BV



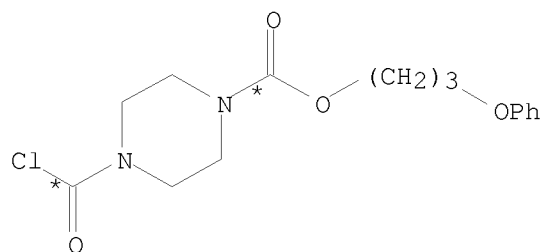
AM



AN

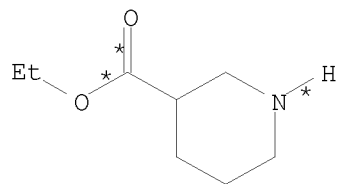
6

STEPS
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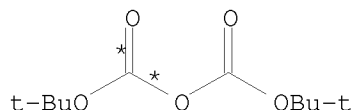


BK

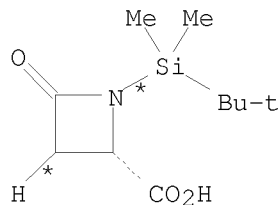
START NEXT REACTION SEQUENCE



AI



AE

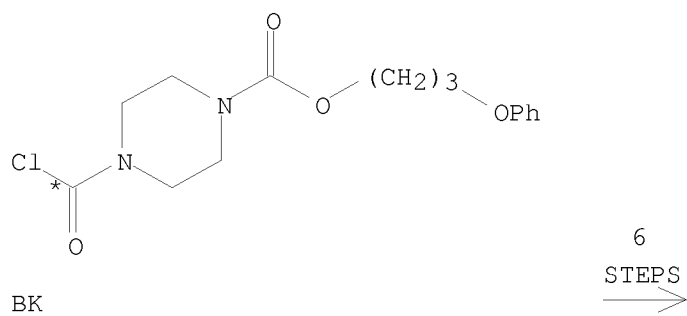
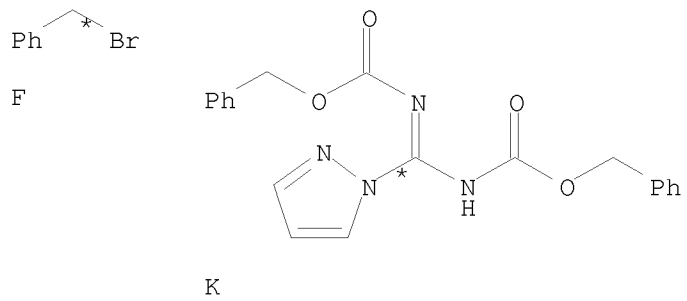


B

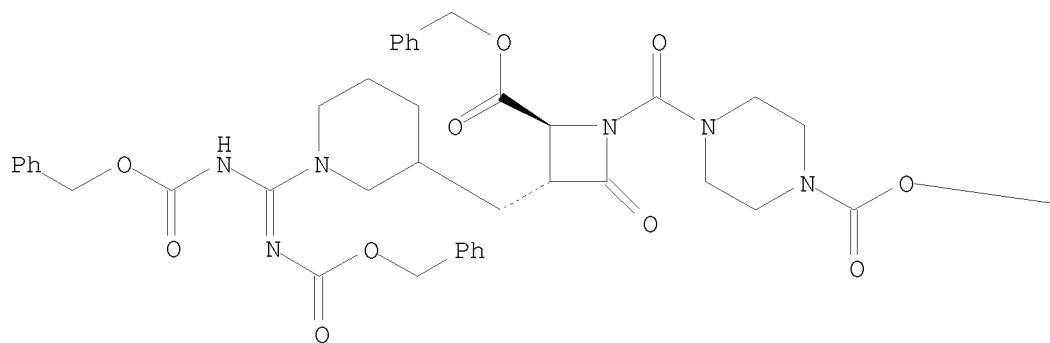
<12/04/2007>

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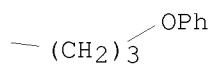


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BL
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH₄
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH₂Cl₂

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)₂
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

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RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N

PRO BL 384830-26-6

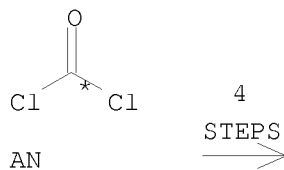
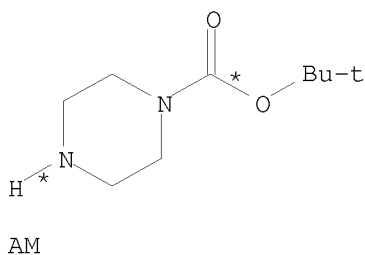
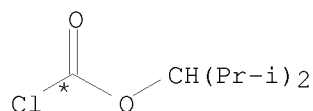
CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

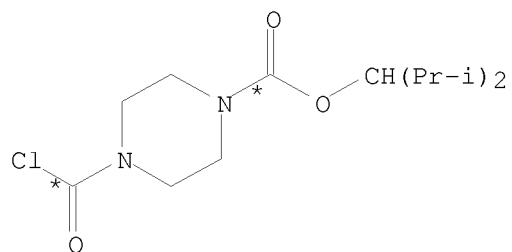
RX(233) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)
AND REACTION SEQUENCE RX(43), RX(16), RX(18), RX(20)

... BR + AM + AN ==> P...

...AH + B + F + K + P ==> BB

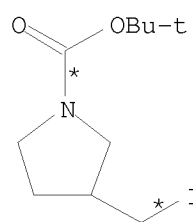


10/513699

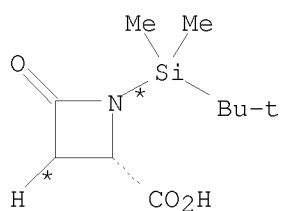


P

START NEXT REACTION SEQUENCE



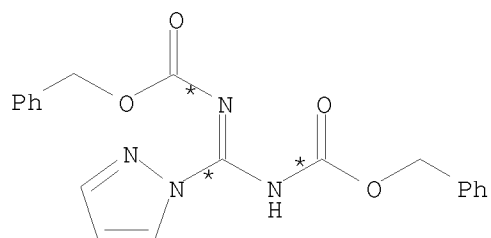
AH



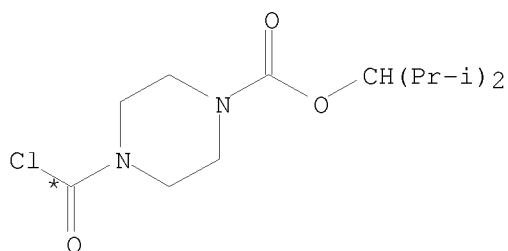
B



F

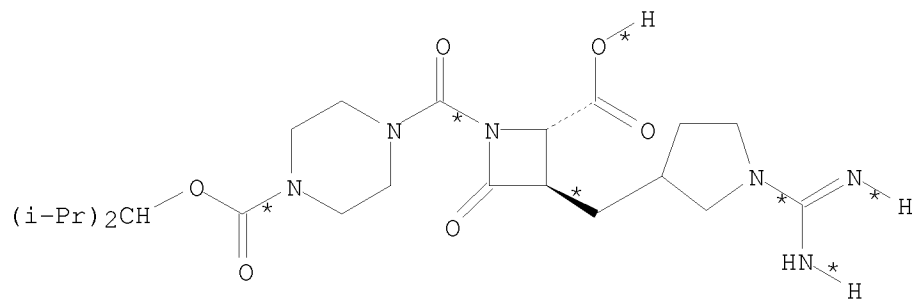


K



P

4
STEPS
→



BB

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RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(43) RCT AH 479622-36-1, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)₂

PRO AX 479622-21-4

SOL 109-99-9 THF

NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)

RGT H 429-41-4 Bu₄N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO₃

SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

PRO BA 479622-23-6

NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

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RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)

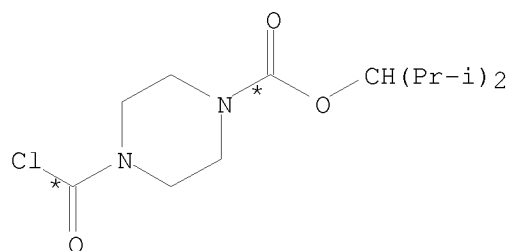
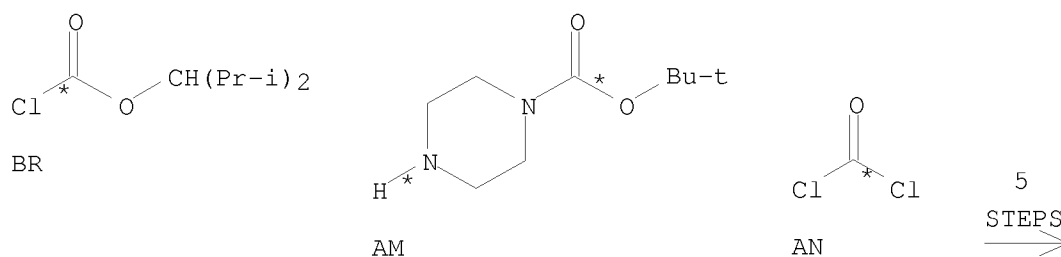
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

RX(234) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)
AND REACTION SEQUENCE RX(8), RX(43), RX(16), RX(18), RX(20)

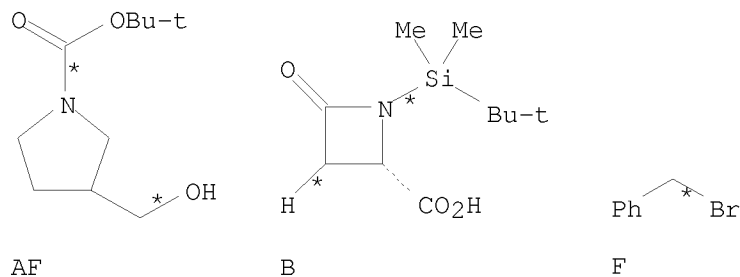
... BR + AM + AN ==> P...

...AF + B + F + K + P ==> BB



P

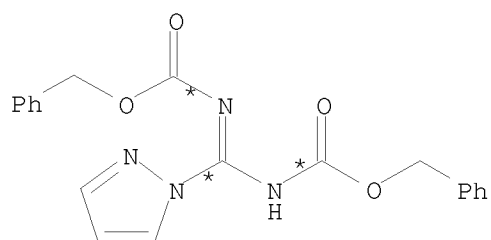
START NEXT REACTION SEQUENCE



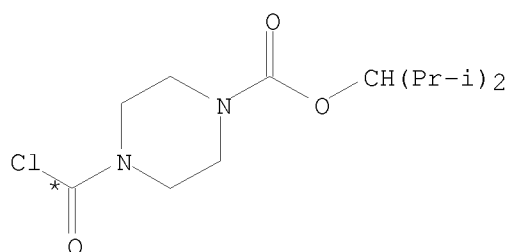
<12/04/2007>

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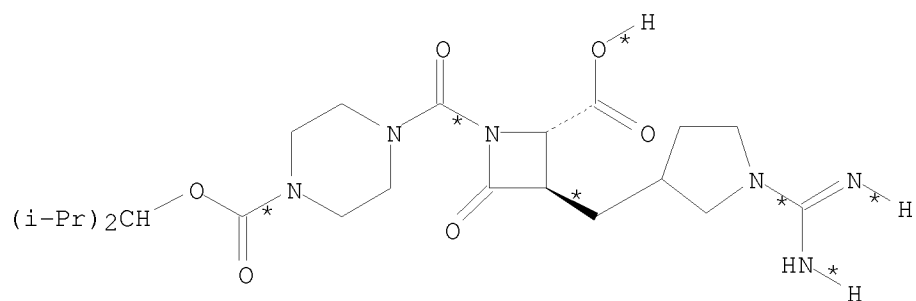


K



P

5
STEPS
→



BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(8) RCT AF 114214-69-6
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AH 479622-36-1
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9

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RGT D 4111-54-0 LiN(Pr-i)2
PRO AX 479622-21-4
SOL 109-99-9 THF
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)
RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO BA 479622-23-6
NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

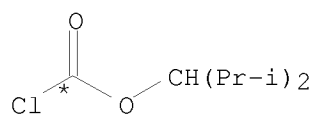
STAGE(2)
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

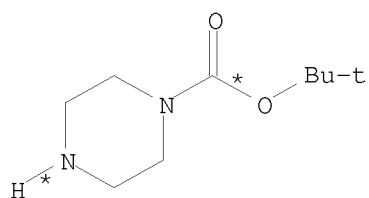
RX(235) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)
AND REACTION SEQUENCE RX(7), RX(8), RX(43), RX(16), RX(18),
RX(20)

... BR + AM + AN ==> P...
...AD + AE + B + F + K + P ==> BB

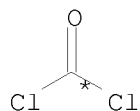
10/513699



BR

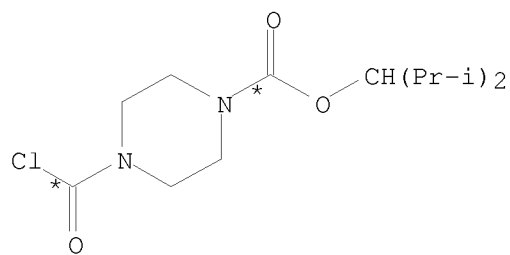


AM



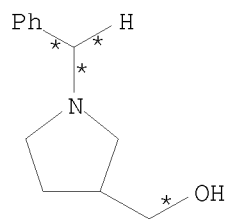
AN

6
STEPS
→

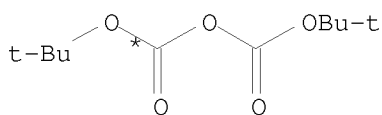


P

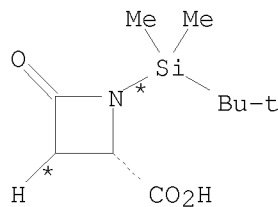
START NEXT REACTION SEQUENCE



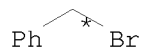
AD



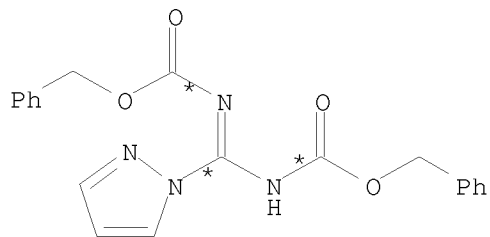
AE



B



F

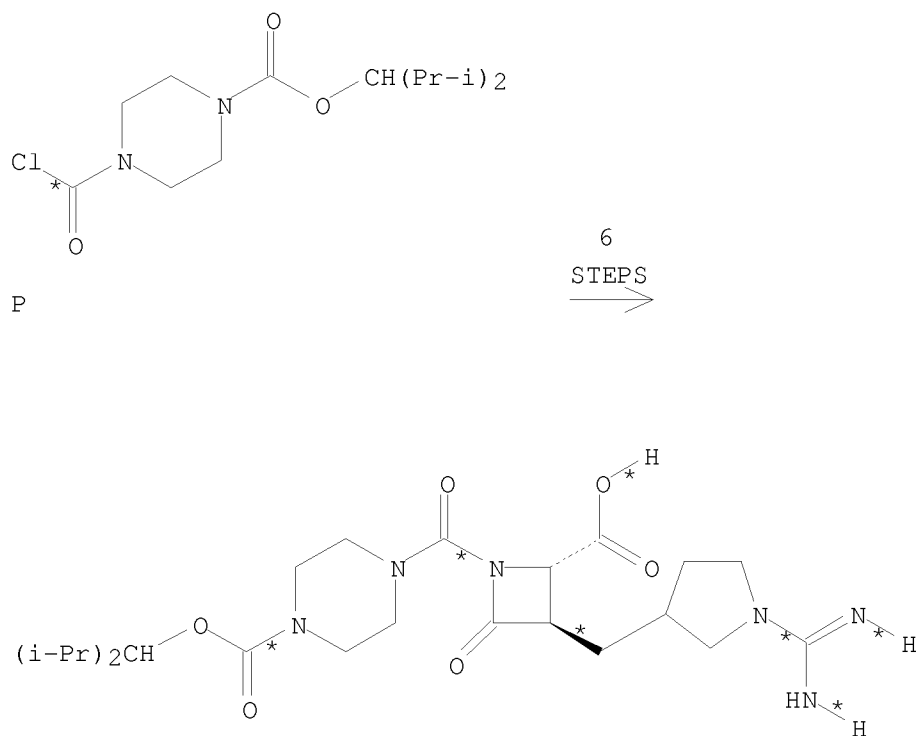


K

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BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3,
alternative prepn. shown

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H₂

CAT 7440-05-3 Pd

SOL 67-56-1 MeOH

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STAGE(2)
RCT AE 24424-99-5
SOL 109-99-9 THF

PRO AF 114214-69-6
NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AH 479622-36-1
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AX 479622-21-4
SOL 109-99-9 THF
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)
RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO BA 479622-23-6
NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP
SOL 68-12-2 DMF

STAGE(2)
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

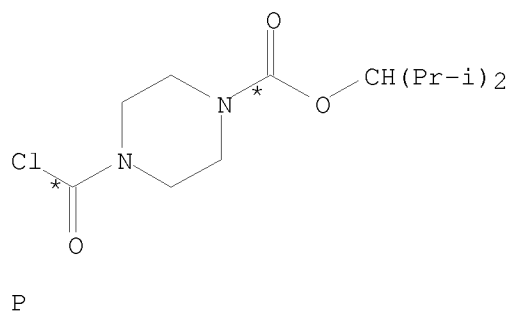
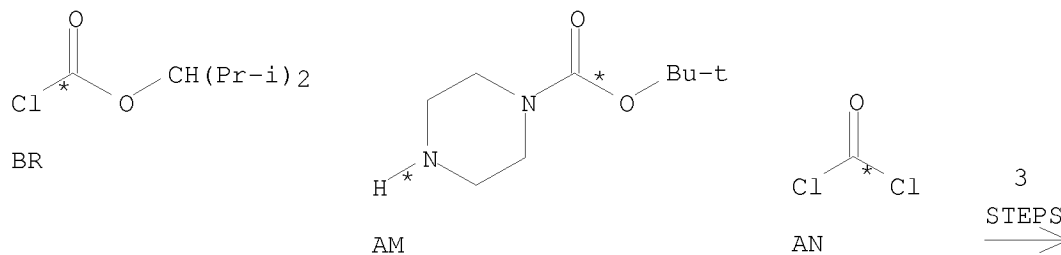
10/513699

PRO BB 479622-24-7

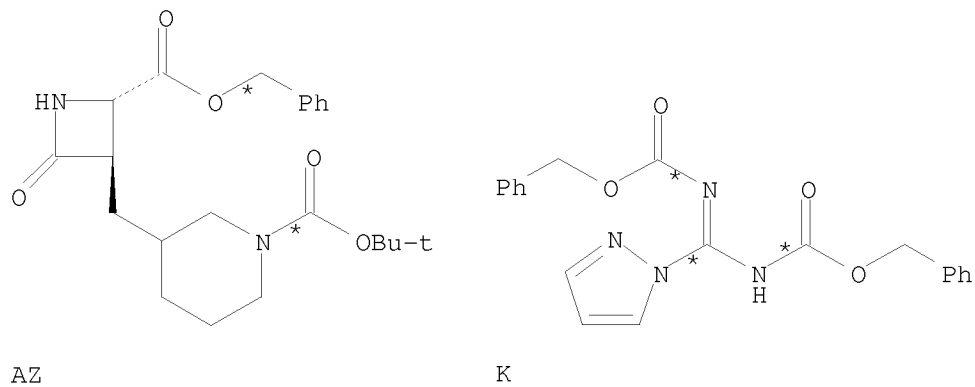
RX(241) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)
AND REACTION SEQUENCE RX(19), RX(5), RX(44)

... BR + AM + AN ==> P...

...AZ + K + P ==> BC



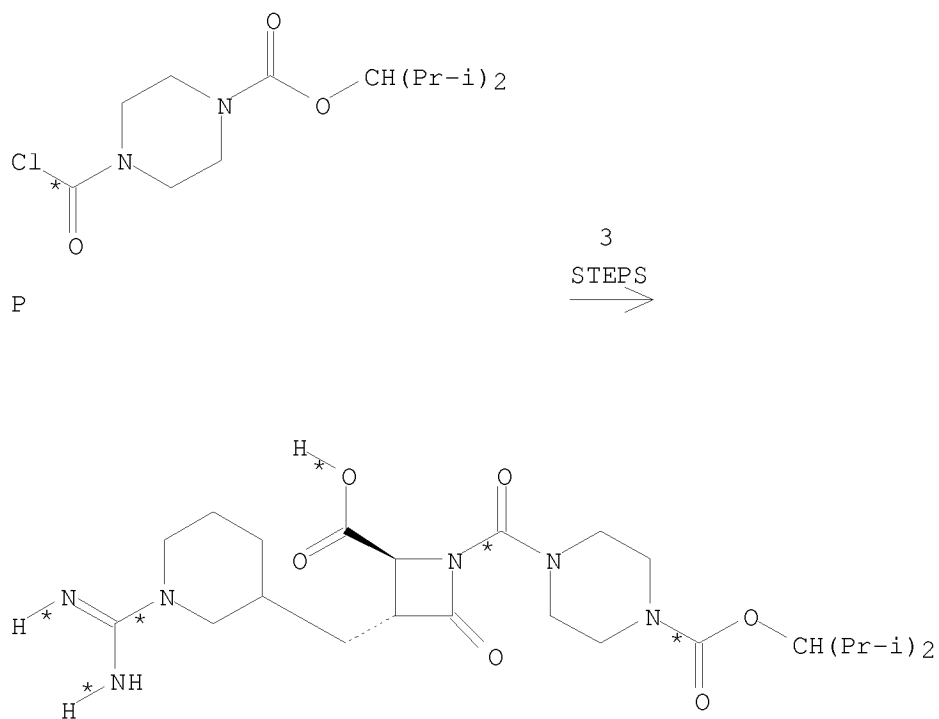
START NEXT REACTION SEQUENCE



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BC
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

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STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

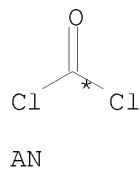
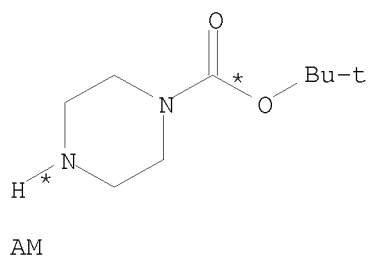
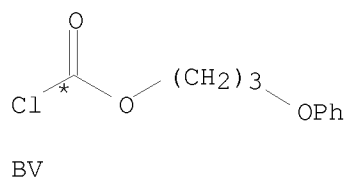
STAGE(2)

SOL 7732-18-5 Water

PRO BC 253177-54-7
NTE polyvinylpyridine resin used in second stage

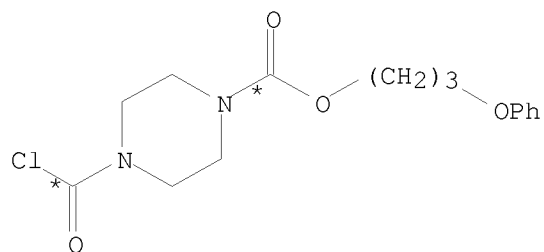
RX(245) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)
AND REACTION SEQUENCE RX(19), RX(25), RX(37)

... BV + AM + AN ==> BK...
...AZ + K + BK ==> BZ



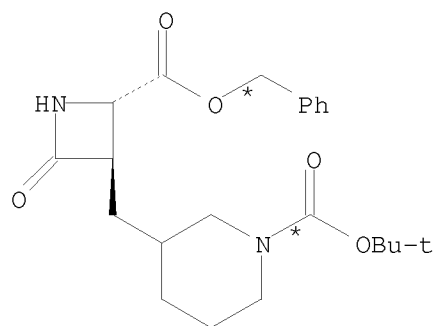
3
STEPS
→

10/513699

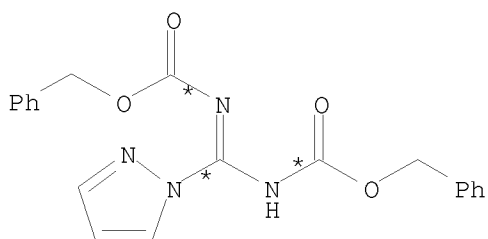


BK

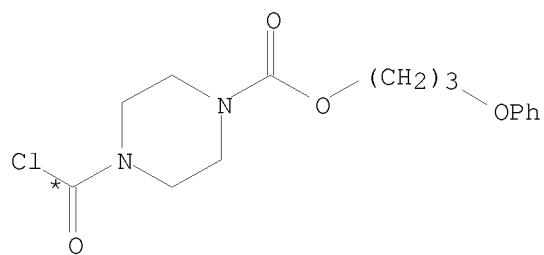
START NEXT REACTION SEQUENCE



AZ



K



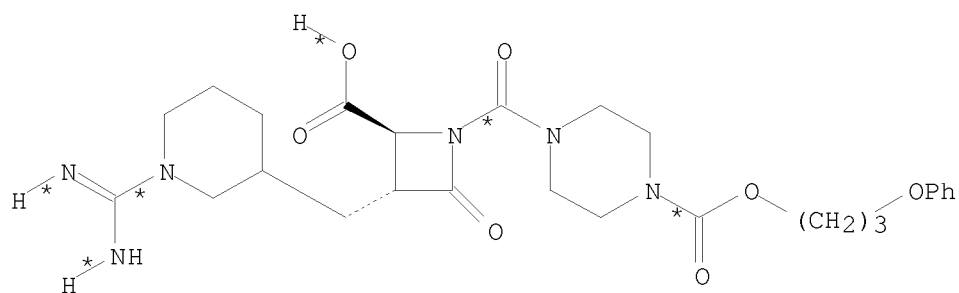
BK

3
STEPS
→

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BZ
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et3N
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

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STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

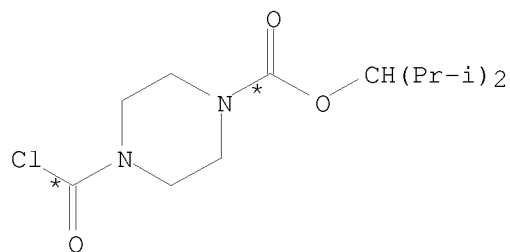
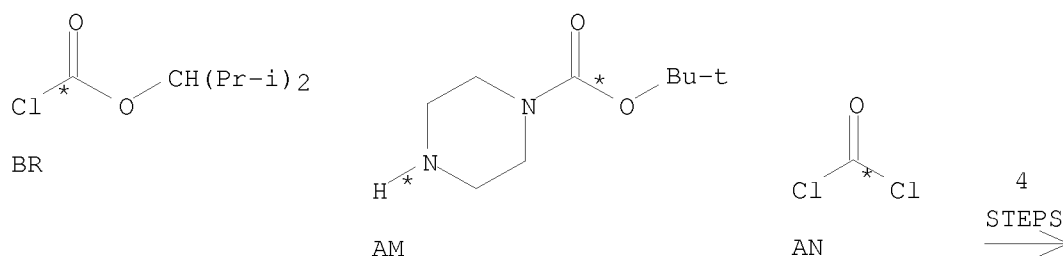
PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

RX(248) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)
AND REACTION SEQUENCE RX(17), RX(19), RX(5), RX(44)

... BR + AM + AN ==> P...

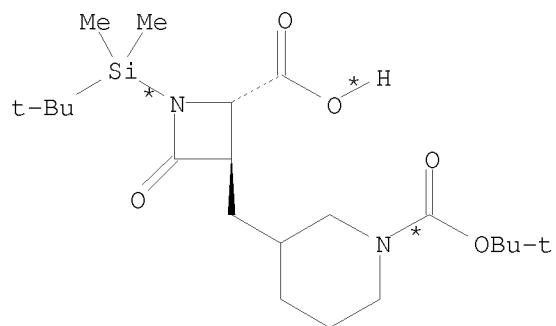
...AW + F + K + P ==> BC



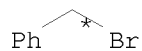
P

START NEXT REACTION SEQUENCE

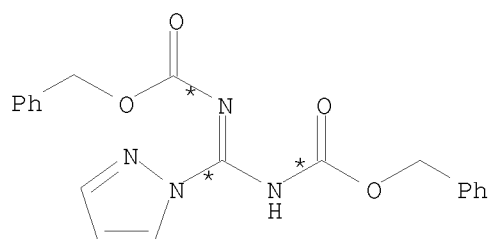
10/513699



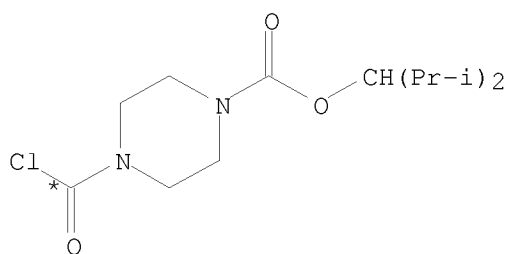
AW



F

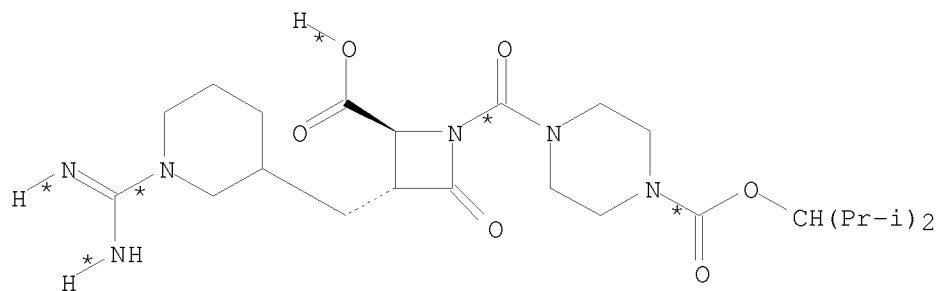


K



P

4
STEPS
→



BC
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

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Erich Leese

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STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

RX(5) RCT P 253177-45-6, X 384830-18-6

RGT N 121-44-8 Et3N

PRO Y 253177-10-5

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

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Erich Leese

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STAGE(2)

SOL 7732-18-5 Water

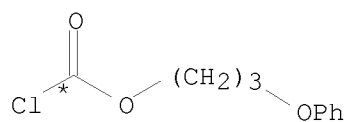
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

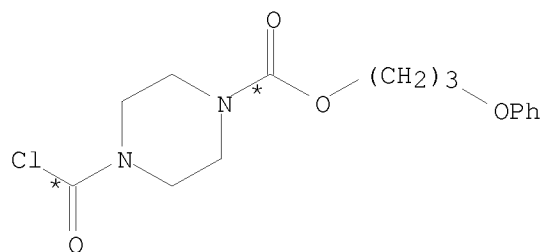
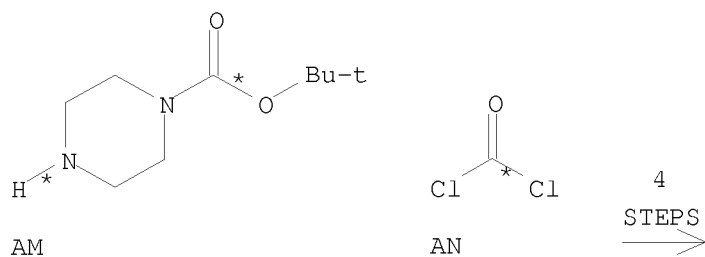
RX(252) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)
AND REACTION SEQUENCE RX(17), RX(19), RX(25), RX(37)

... BV + AM + AN ==> BK...

...AW + F + K + BK ==> BZ



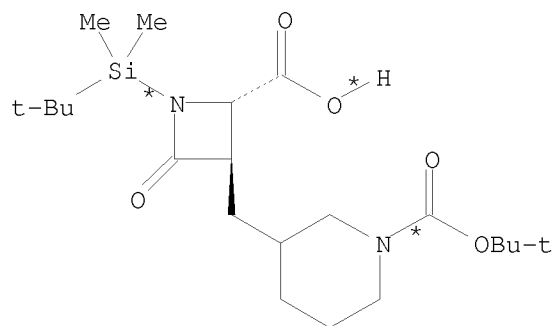
BV



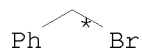
BK

START NEXT REACTION SEQUENCE

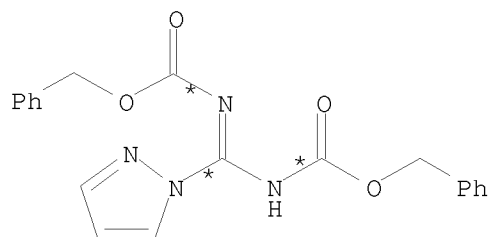
10/513699



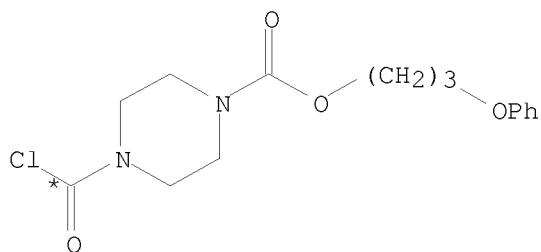
AW



F

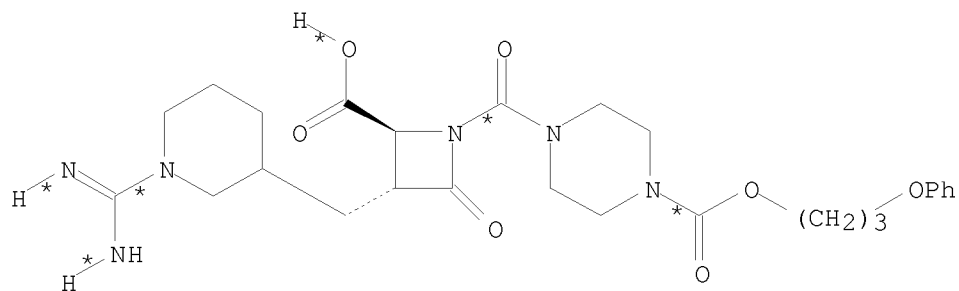


K



BK

4
STEPS
→



BZ
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

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STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu₄N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO₃
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et₃N

PRO BL 384830-26-6

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H₂, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

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STAGE(2)

SOL 7732-18-5 Water

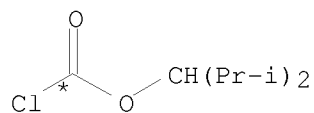
PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

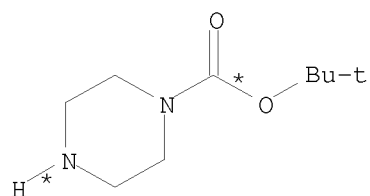
RX(255) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(5), RX(44)

... BR + AM + AN ==> P...

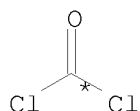
...AL + B + F + K + P ==> BC



BR

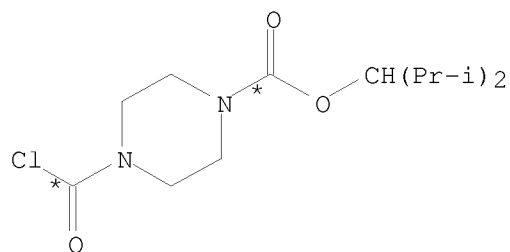


AM



AN

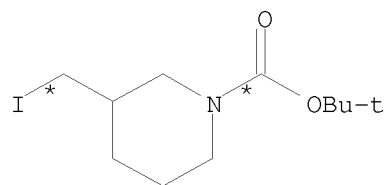
5
STEPS
→



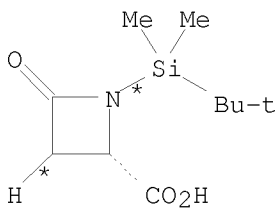
P

START NEXT REACTION SEQUENCE

10/513699



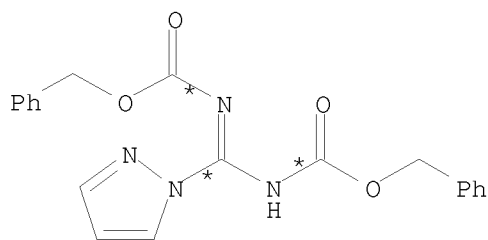
AL



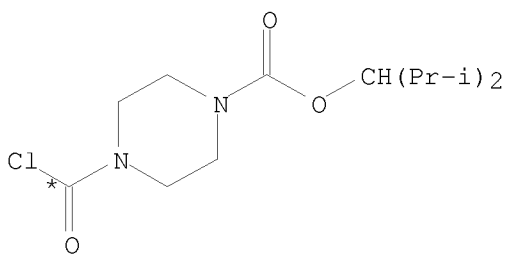
B



F

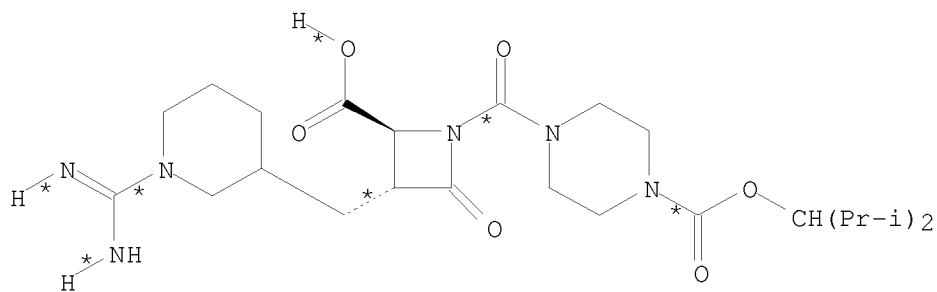


K



P

5
STEPS
→



BC
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

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STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd

<12/04/2007>

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SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

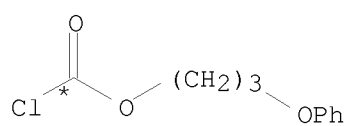
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

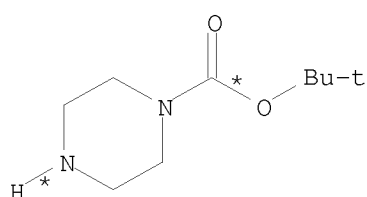
RX(259) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(25), RX(37)

... BV + AM + AN ==> BK...

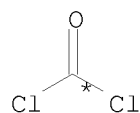
...AL + B + F + K + BK ==> BZ



BV

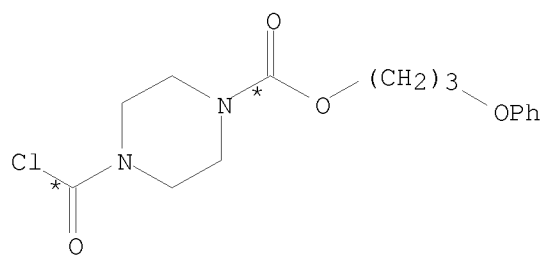


AM



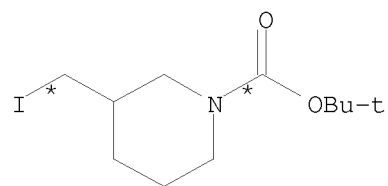
AN

5
STEPS
→

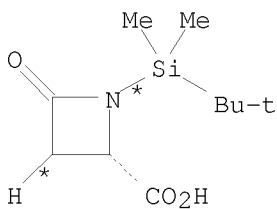


BK

START NEXT REACTION SEQUENCE



AL



B

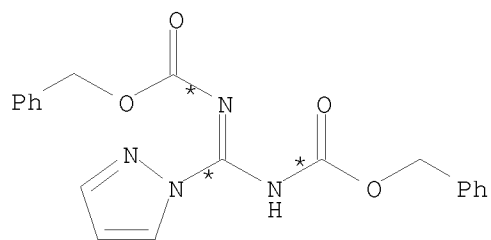


F

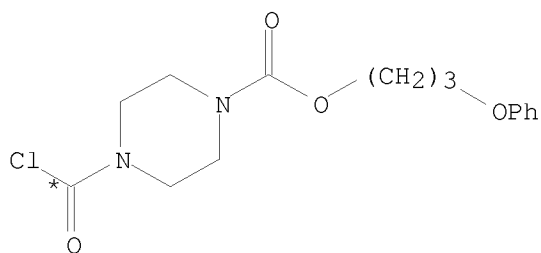
<12/04/2007>

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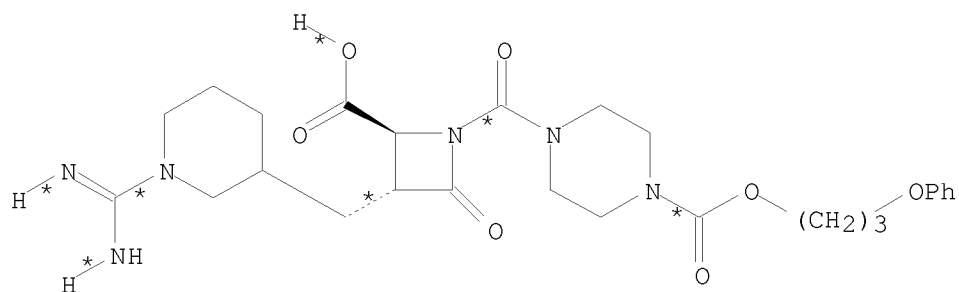


K



BK

5
STEPS
→



BZ
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative

<12/04/2007>

Erich Leese

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prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et3N
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

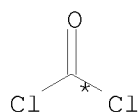
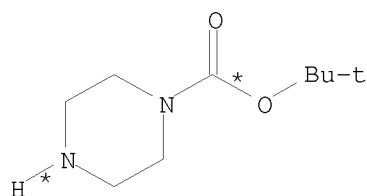
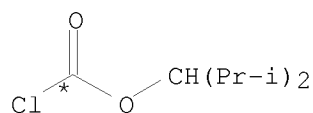
RX(262) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(5),

<12/04/2007>

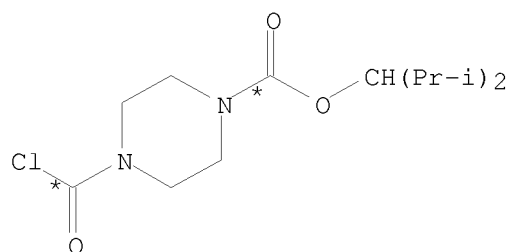
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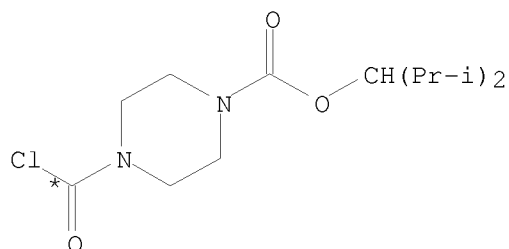
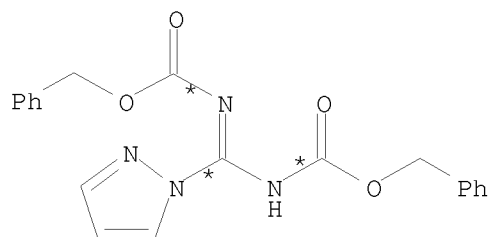
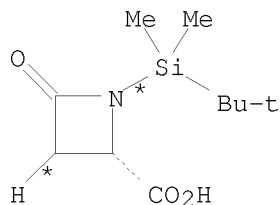
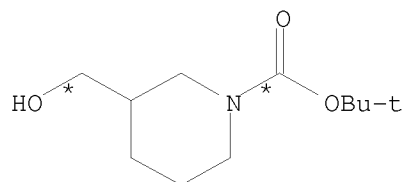
RX(44)
... BR + AM + AN ==> P...
...AJ + B + F + K + P ==> BC



6
STEPS
→



START NEXT REACTION SEQUENCE

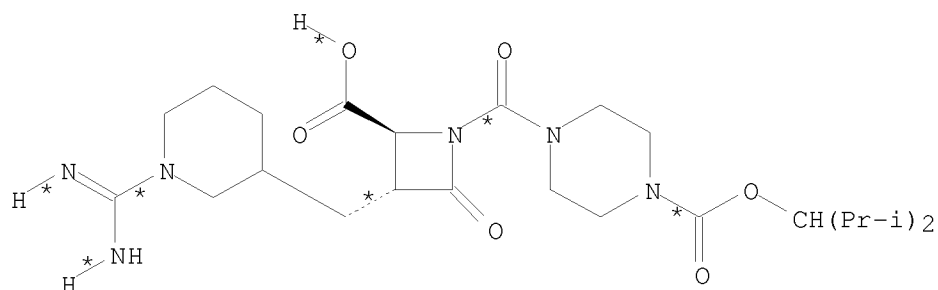


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6
STEPS
→



BC
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et₃N

SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(10)

RCT AJ 116574-71-1

RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole

PRO AL 253177-03-6

SOL 75-09-2 CH₂Cl₂

RX(15)

RCT AL 253177-03-6, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)₂

PRO AW 253177-04-7

SOL 109-99-9 THF

NTE stereoselective

RX(17)

RCT AW 253177-04-7

STAGE(1)

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RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

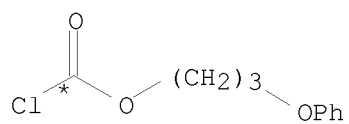
SOL 7732-18-5 Water

PRO BC 253177-54-7
NTE polyvinylpyridine resin used in second stage

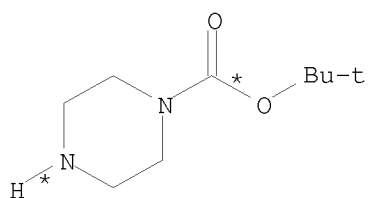
RX(266) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(25),
RX(37)

... BV + AM + AN ==> BK...
...AJ + B + F + K + BK ==> BZ

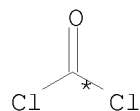
10/513699



BV

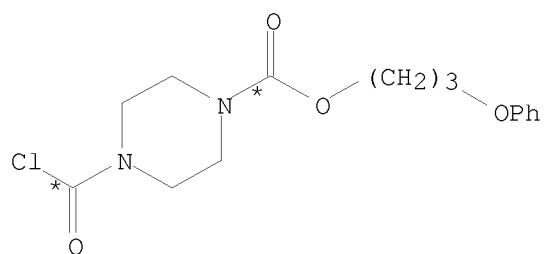


AM



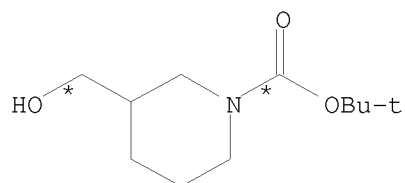
AN

6
STEPS
→

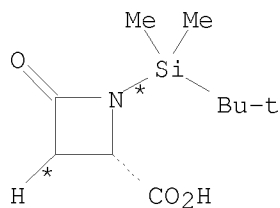


BK

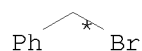
START NEXT REACTION SEQUENCE



AJ



B

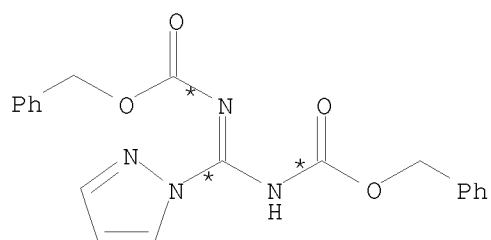


F

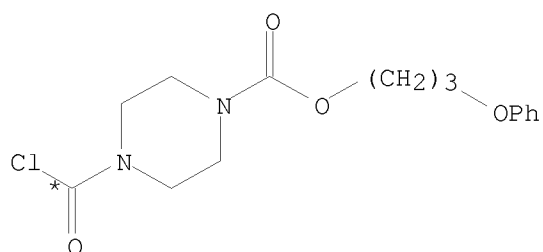
<12/04/2007>

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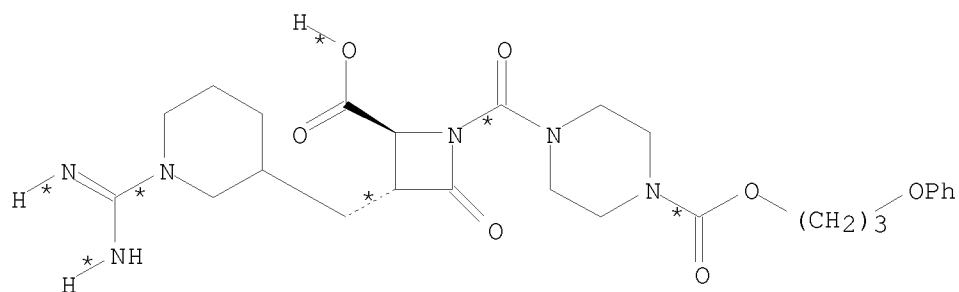


K



BK

6
STEPS
→



BZ
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

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RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)
RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)
RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et3N
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)
RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)
SOL 7732-18-5 Water

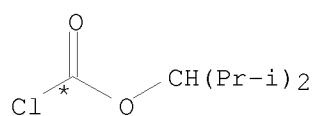
PRO BZ 384829-80-5
NTE polyvinylpyridine resin used in second stage

10/513699

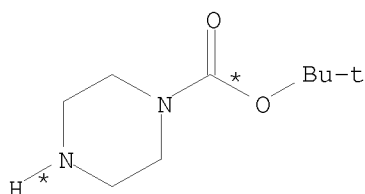
RX(271) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),
RX(5), RX(44)

... BR + AM + AN ==> P...

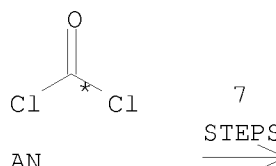
...AI + AE + B + F + K + P ==> BC



BR

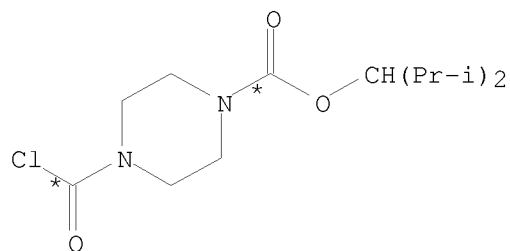


AM



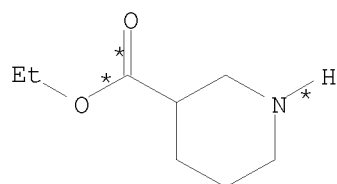
AN

7
STEPS
→

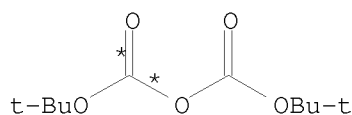


P

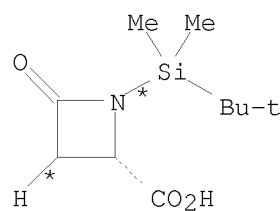
START NEXT REACTION SEQUENCE



AI

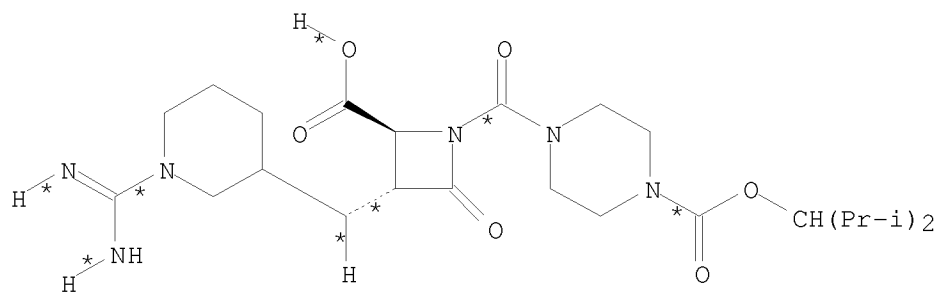
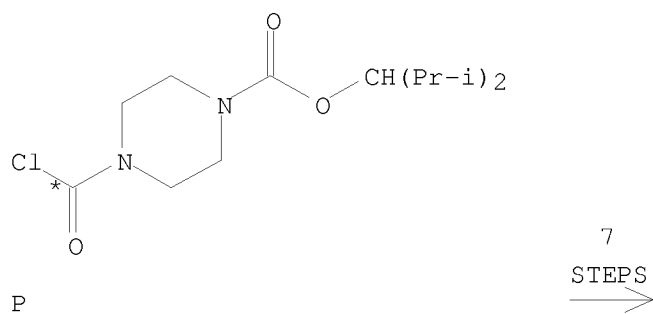
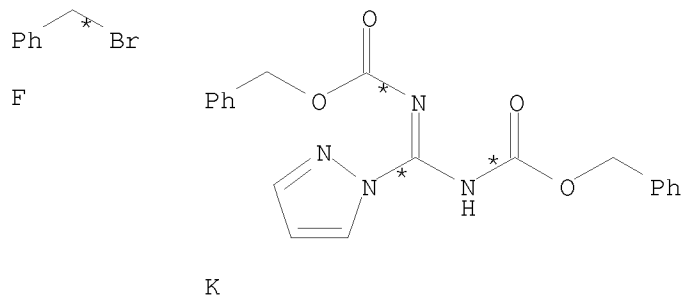


AE



B

10/513699



BC
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et₃N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F₃CCO₂H

SOL 75-09-2 CH₂Cl₂

STAGE(3)

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RCT AN 75-44-5
RGT N 121-44-8 Et₃N
SOL 75-09-2 CH₂Cl₂

PRO P 253177-45-6
NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)
SOL 109-99-9 THF

STAGE(2)
RGT AK 16853-85-3 LiAlH₄
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1
RGT AA 7553-56-2 I₂, AB 603-35-0 PPh₃, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH₂Cl₂

RX(15) RCT AL 253177-03-6, B 82938-50-9
RGT D 4111-54-0 LiN(Pr-i)₂
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)
RGT H 429-41-4 Bu₄N.F
SOL 109-99-9 THF

STAGE(2)
RCT F 100-39-0
RGT I 144-55-8 NaHCO₃
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)
RGT M 76-05-1 F₃CCO₂H
SOL 75-09-2 CH₂Cl₂

STAGE(2)
RCT K 152120-55-3
RGT N 121-44-8 Et₃N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

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RX(5) RCT P 253177-45-6, X 384830-18-6
RGT N 121-44-8 Et3N
PRO Y 253177-10-5
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

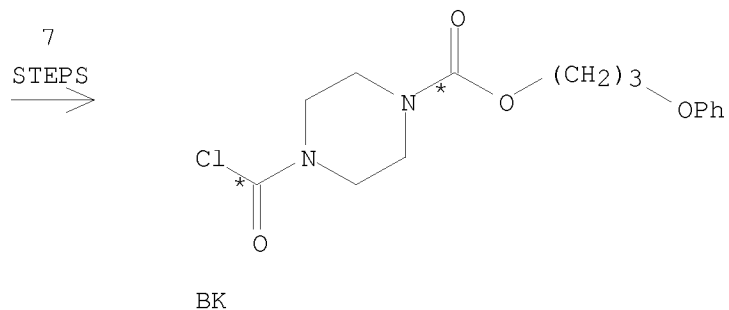
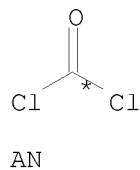
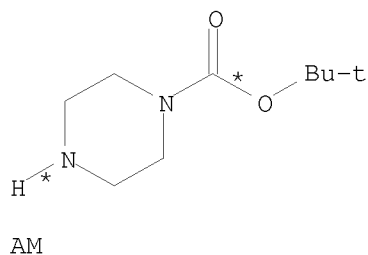
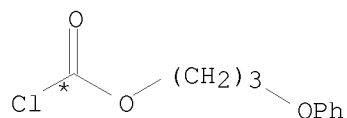
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

RX(275) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),
RX(25), RX(37)

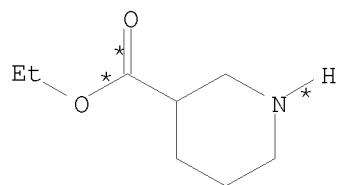
... BV + AM + AN ==> BK...

...AI + AE + B + F + K + BK ==> BZ

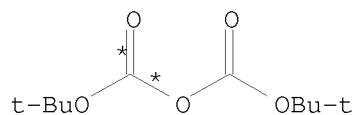


START NEXT REACTION SEQUENCE

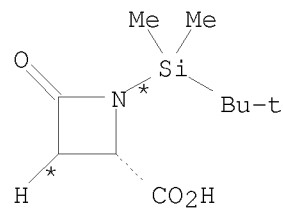
10/513699



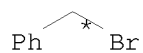
AI



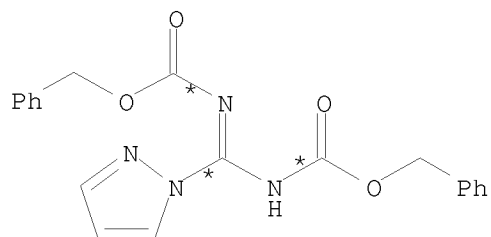
AE



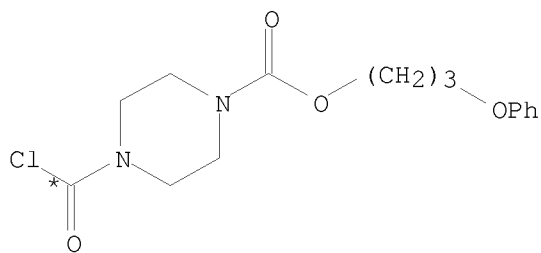
B



F

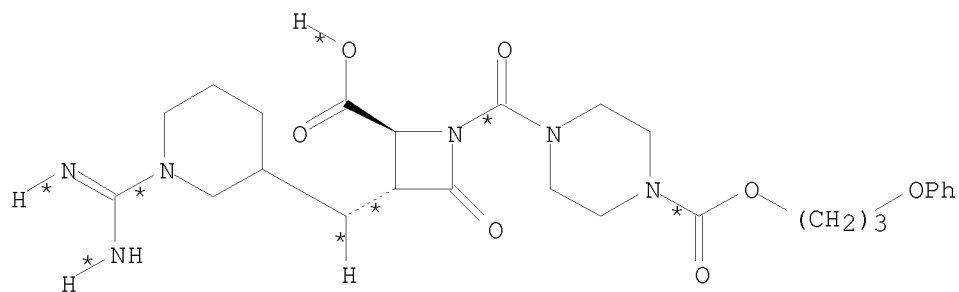


K



BK

7
STEPS
→



BZ
YIELD 92%

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RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5
RGT N 121-44-8 Et3N
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH4
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1

RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
PRO AL 253177-03-6
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2
PRO AW 253177-04-7
SOL 109-99-9 THF
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0
RGT I 144-55-8 NaHCO3
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

10/513699

RGT M 76-05-1 F3CCO2H
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3
RGT N 121-44-8 Et3N
SOL 68-12-2 DMF

PRO X 384830-18-6
NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6
RGT N 121-44-8 Et3N
PRO BL 384830-26-6
CAT 1122-58-3 4-DMAP
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl
CAT 7440-05-3 Pd
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

SO Bioorganic & Medicinal Chemistry Letters (2002), 12(21),
3235-3238
CODEN: BMCLE8; ISSN: 0960-894X

10/513699

=> d ih

'IH' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE, Single-step Reactions
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- Indexing data
IPC ----- International Patent Classifications
ISTD ----- STD, indented with text labels
OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

MAX ----- Same as ALL
PATS ----- PI, SO
SCAN ----- TI and FCRD (random display, no answer number. SCAN
must be entered on the same line as DISPLAY, e.g.,
D SCAN.)
SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for
all single-step reactions)
STD ----- BIB, IPC, and NCL

CRD ----- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ----- Reaction Map, Diagram, and Summary for first
hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ----- First hit in Compact Reaction Display (CRD) format
FCRDREF ----- First hit in Compact Reaction Display (CRD) format with
CA reference information (SO, PY). (Default)
FPATH ----- PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT ----- Reaction Map, Reaction Diagram, and Reaction
Summary for all hit reactions and fields containing
hit terms
OCC ----- All hit fields and the number of occurrences of the
hit terms in each field. Includes total number of
HIT, PATH, SPATH reactions. Labels reactions that have
incomplete verifications.
PATH ----- Reaction Map and Reaction Diagram for the "long
path". Displays all hit reactions, except those
whose steps are totally included within another hit
reaction which is displayed
RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)

<12/04/2007>

Erich Leese

RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
 RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)
 SPATH ----- Reaction Map and Reaction Diagram for the "short
 path". Displays all single step reactions which
 contain a hit substance. Also displays those
 multistep reactions that have a hit substance in both
 the first and last steps of the reaction, except for
 those hit reactions whose steps are totally included
 within another hit reaction which is displayed

To display a particular field or fields, enter the display field
 codes. For a list of the display field codes, enter HELP DFIELDS
 at an arrow prompt (=>). Examples of combinations include: D TI;
 D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
 as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
 FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
 be used with the DISPLAY command to display the record for a specified
 Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):d his
 'D' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS ----- GI and AB
 ALL ----- BIB, AB, IND, RE, Single-step Reactions
 APPS ----- AI, PRAI
 BIB ----- AN, plus Bibliographic Data
 CAN ----- List of CA abstract numbers without answer numbers
 CBIB ----- AN, plus Compressed Bibliographic Data
 DALL ----- ALL, delimited (end of each field identified)
 IABS ----- ABS, indented with text labels
 IALL ----- ALL, indented with text labels
 IBIB ----- BIB, indented with text labels
 IND ----- Indexing data
 IPC ----- International Patent Classifications
 ISTD ----- STD, indented with text labels
 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

 MAX ----- Same as ALL
 PATS ----- PI, SO
 SCAN ----- TI and FCRD (random display, no answer number. SCAN
 must be entered on the same line as DISPLAY, e.g.,
 D SCAN.)
 SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for
 all single-step reactions)
 STD ----- BIB, IPC, and NCL

 CRD ----- Compact Display of All Hit Reactions
 CRDREF ----- Compact Reaction Display and SO, PY for Reference
 FHIT ----- Reaction Map, Diagram, and Summary for first
 hit reaction
 FHITCBIB --- FHIT, AN plus CBIB

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FCRD ----- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
 CA reference information (SO, PY). (Default)
FPATH ----- PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT ----- Reaction Map, Reaction Diagram, and Reaction
 Summary for all hit reactions and fields containing
 hit terms
OCC ----- All hit fields and the number of occurrences of the
 hit terms in each field. Includes total number of
 HIT, PATH, SPATH reactions. Labels reactions that have
 incomplete verifications.
PATH ----- Reaction Map and Reaction Diagram for the "long
 path". Displays all hit reactions, except those
 whose steps are totally included within another hit
 reaction which is displayed
RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)
SPATH ----- Reaction Map and Reaction Diagram for the "short
 path". Displays all single step reactions which
 contain a hit substance. Also displays those
 multistep reactions that have a hit substance in both
 the first and last steps of the reaction, except for
 those hit reactions whose steps are totally included
 within another hit reaction which is displayed

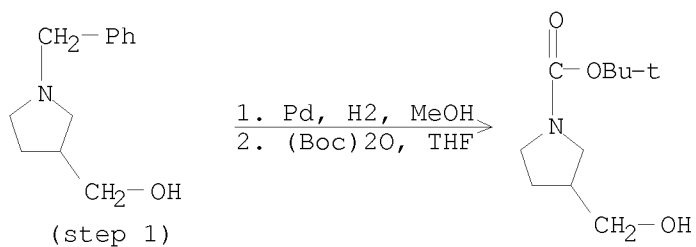
To display a particular field or fields, enter the display field
codes. For a list of the display field codes, enter HELP DFIELDS
at an arrow prompt (=>). Examples of combinations include: D TI;
D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
be used with the DISPLAY command to display the record for a specified
Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):
ENTER DISPLAY FORMAT (FCRDREF):.

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L10 ANSWER 1 OF 1 CASREACT COPYRIGHT 2008 ACS on STN

RX(7) OF 275



REF: Bioorganic & Medicinal Chemistry Letters, 12(21), 3235-3238; 2002

NOTE: isopropanol may also be used as a solvent in the first stage

<12/04/2007>

Erich Leese

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=> d his

(FILE 'HOME' ENTERED AT 11:16:01 ON 01 FEB 2008)

FILE 'REGISTRY' ENTERED AT 11:16:18 ON 01 FEB 2008

L1 STRUCTURE UPLOADED

L2 37 S L1 FULL

FILE 'CAPLUS' ENTERED AT 11:16:56 ON 01 FEB 2008

L3 17 S L2 FULL

L4 17 S L3 AND PY<2003

FILE 'CASREACT' ENTERED AT 11:30:01 ON 01 FEB 2008

L5 STRUCTURE UPLOADED

L6 10 S L5

L7 197 S L5 FULL

L8 93 S L7 AND PY<2003

L9 0 S L8 AND ORGANIC SOLVENT

L10 1 S L8 AND SOLVENT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	140.47	423.89
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-14.35

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FILE CONTAINS CURRENT INFORMATION.

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FULL ESTIMATED COST	0.12	424.01
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-14.35

STN INTERNATIONAL LOGOFF AT 11:37:24 ON 01 FEB 2008